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STIFLING OR STIMULATING—THE ROLE OF GENE PATENTS IN RESEARCH AND GENETIC TESTING

HEARING

BEFORE THE

SUBCOMMITTEE ON COURTS, THE INTERNET,
AND INTELLECTUAL PROPERTY

OF THE

COMMITTEE ON THE JUDICIARY
HOUSE OF REPRESENTATIVES

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CONTENTS

OCTOBER 30, 2007

Page

OPENING STATEMENTS

The Honorable Howard L. Berman, a Representative in Congress from the State of California, and Chairman, Subcommittee on Courts, the Internet, and Intellectual Property 1
The Honorable Howard Coble, a Representative in Congress from the State of North Carolina, and Ranking Member, Subcommittee on Courts, the Internet, and Intellectual Property 4

WITNESSES

Mr. Lawrence M. Sung, J.D., Ph.D., Law School Professor and Intellectual Property Law Program Director, University of Maryland, School of Law, Baltimore, MD
  Oral Testimony 7
  Prepared Statement 10
Mr. E. Jonathan Soderstrom, Managing Director, Office of Cooperative Research, Yale University, New Haven, CT
  Oral Testimony 24
  Prepared Statement 26
Dr. Marc Grodman, Chair of the Board and CEO, Bio-Reference Laboratories, Elmwood Park, NJ
  Oral Testimony 34
  Prepared Statement 37
Mr. Jeffrey Kushan, Partner, Sidley Austin, LLP, on behalf of Biotechnology Industry Organzation (BIO), Washington, DC
  Oral Testimony 57
  Prepared Statement 59

LETTERS, STATEMENTS, ETC., SUBMITTED FOR THE HEARING

Prepared Statement of the Honorable Howard L. Berman, a Representative in Congress from the State of California, and Chairman, Subcommittee on Courts, the Internet, and Intellectual Property 3
Prepared Statement of the Honorable Howard Coble, a Representative in Congress from the State of North Carolina, and Ranking Member, Subcommittee on Courts, the Internet, and Intellectual Property 5

Page

APPENDIX

Material Submitted for the Printed Hearing Record 117

OFFICIAL HEARING RECORD

MATERIAL SUBMITTED FOR THE HEARING RECORD BUT NOT REPRINTED

A publication of the National Research Council of the National Academies entitled "Reaping the Benefits of Genomic and Proteomic Research, Intellectual Property Rights, Innovation, and Public Health." This publication is available at the Subcommittee and can also be accessed at:

http://www.nap.edu/catalog.php?record_id=11487#toc

A report entitled "The Better World Report *Part One*, Building a Stronger Economy: Profiles of 25 Companies Rooted in Academic Research, 2007 Edition." This report is available at the Subcommittee and can also be accessed at:

http://www.betterworldproject.net/documents/AUTMBWR1.pdf

A report entitled "Technology Transfer Stories: 25 Innovations That Changed the World, The Better World Report, 2006 Edition." This report is available at the Subcommittee and can also be accessed at:

http://www.betterworldproject.net/documents/AUTM_BWR.pdf

STIFLING OR STIMULATING—THE ROLE OF GENE PATENTS IN RESEARCH AND GENETIC TESTING

TUESDAY, OCTOBER 30, 2007

House of Representatives,
Subcommittee on Courts, the Internet,
and Intellectual Property,
Committee on the Judiciary,
Washington, DC.

The Subcommittee met, pursuant to notice, at 2:14 p.m., in Room 2237, Rayburn House Office Building, the Honorable Howard L. Berman (Chairman of the Subcommittee) presiding.

Present: Representatives Berman, Watt, Lofgren, Coble, and Issa.

Staff present: Shanna Winters, Subcommittee Majority Chief Counsel; Eric Garduno, Majority Counsel; Blaine Merritt, Minority Counsel; and Rosalind Jackson, Professional Staff Member.

Mr. Berman. Good afternoon. The hearing of the Subcommittee on Courts, the Internet, and Intellectual Property will come to order.

I would like to begin by welcoming everyone to this hearing, "Stifling or Stimulating—The Role of Gene Patents in Research and Genetic Testing."

I noticed a couple of days ago that George Bush, when he was talking about President Putin and some of the problems in Russia, he said that in terms of whether or not it is possible to reprogram the kind of basic Russian DNA, which is used to centralized authority, that is hard to do, and so I would first like to know if there is a patent for an authoritarian gene, and how does it express itself, and can it be licensed? [Laughter.]

Scientific knowledge concerning genes has expanded considerably in the last half-century since James Watson and Francis Crick put forth their discovery of DNA.

We know now that genes are the blueprints of all living things. I am told that genes are chemical instructions stored in our cells that tell our bodies to grow bones, make blood, repair damaged skin, and perform tens of thousands of other functions.

Efforts to map the human genome, like the Human Genome Project headed by NIH, have allowed us to identify specific genes, determine their function, and harness their usefulness. As a result, we have been able to produce therapies to alleviate human suffering, such as insulin, develop tests to determine susceptibility to diseases, like Alzheimer's and breast cancer, and create wholly new organisms, like cancer mice and pesticide-resistant plants.

Many attribute this success to the incentives provided by the patent system. Given the robust nature of the commercialization of biotechnology research, it is fair to say that patents have done their job in promoting new inventions in this field. However, there are those that have raised concerns about the impact of providing exclusivity for patents on genes.

For some, genes are thought of as products of nature and, thus, should not be patentable subject matter. However, the courts have long held that compositions of matter isolated and purified from their natural state are worthy of patent protection. This principle was made clearly applicable to living matter like genes in the Supreme Court's *Diamond v. Chakrabarty* decision.

For some, gene patents should require a more rigorous review. The USPTO revised their examination guidelines for gene patenting in 2001, which strengthened utility requirements so that a gene could no longer be patented based on uses like being good for landfill.

But while the 2001 guidelines tightened patentability requirements, some continue to argue that many gene patents are still issued for uses that are speculative and unproven.

If the quality of gene patents remain a problem, stricter utility standards requiring more concrete uses may be called for. However, any lingering quality issues surrounding how gene inventions are examined could very well be impacted by the recent *KSR v. Teleflex* decision.

I know at least one of our witnesses will be speaking to that issue.

Still, others fear that gene patents will be used to hinder research. They argue that if patent thickets were to form, it would become too costly or too troublesome for researchers to license the patented inventions they need, forcing them to abandon their research. There is anecdotal information that supports this notion that researchers have discontinued research pursuits because of the threat of lawsuits by gene patent holders. However, there is also data that suggests just the opposite, that gene patents have had little impact on basic research.

A recent survey by the National Academy of Sciences found that in biomedical research, "There is a lack of substantial evidence for a patent thicket or a patent blocking problem," primarily because researchers are not very concerned about patents being enforced against them. However, the report went on to say that this nonchalant attitude was based on the assumption by many researchers that they qualify for a robust research use exception, which many believe was eliminated by the 2002 *Madey v. Duke* decision.

Regardless, it might only take one major victory against a university to create a real and substantial chilling effect. As such, we may need to examine the effects or necessity of a clear research use exception.

Finally, for some, opposition to gene patents is a matter of principle. They point out that patents on genetic tests is harming patient access to and stunting improvement of these tests. It is reasoned that since most insurance providers do not provide coverage for genetic tests, the patent markup can price tests out of reach for many patients.

In addition, some claim that gene patents have been asserted in order to prevent others from improving possibly inaccurate genetic tests and identifying whether these are even applicable to certain population subgroups.

While I firmly support a patent holder's right to charge what the market will bear for his invention, using a patent to block efforts that check the efficacy of such tests borders on the realm of patent misuse and may constitute anti-competitive practices.

Patents are meant to encourage technological progress. Thus, it is antithetical to the patent system for companies to use their patents to freeze a technology at a particular stage of development.

But is that what is happening? Are the practices of a few unfairly coloring all gene patents in a negative light? Are complaints related to gene patents based more on how they are being used instead of what is being patented?

We need to examine the role gene patents play in stimulating or stifling research in genetic testing. It is my hope that this hearing will help us answer these and many other underlying questions.

It is now my pleasure to recognize my friend and colleague, the distinguished Ranking minority Member of the Subcommittee, Howard Coble, for his opening statement.

[The prepared statement of Mr. Berman follows:]

PREPARED STATEMENT OF THE HONORABLE HOWARD L. BERMAN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF CALIFORNIA, AND CHAIRMAN, SUBCOMMITTEE ON COURTS, THE INTERNET, AND INTELLECTUAL PROPERTY

Scientific knowledge concerning genes has expanded considerably in the last half century since James Watson and Francis Crick put forth their discovery of DNA. We now know that genes are the blueprints of all living things. Efforts to map the human genome like the Human Genome Project headed by NIH has allowed us to identify specific genes, determine their function, and harness their usefulness. As a result we have been able to produce therapies to alleviate human suffering such as insulin, develop tests to determine susceptibility to diseases like Alzheimer's and breast cancer, and create wholly new organisms like "cancer mice" and pesticide resistant plants.

Many attribute this success to the incentives provided by the patent system. Given the robust nature of the commercialization of biotechnology research, it's fair to say that patents have done their job in promoting new inventions in this field. However, there are those that have raised concerns about the impact of providing exclusivity for patents on genes.

For some, genes are thought of as products of nature and thus should not be patentable subject matter. However, the courts have long held that compositions of matter isolated and purified from their natural state are worthy of patent protection. This principle was made clearly applicable to living matter like genes thanks to the Supreme Court's *Diamond v. Chakrabarty* decision.

For some, gene patents should require a more rigorous review. The USPTO revised their examination guidelines for gene patenting in 2001, which strengthened utility requirements so that a gene could no longer be patented based on uses like being "good for landfill." But, while the 2001 guidelines tightened patentability requirements, some continue to argue that many gene patents are still issued for uses that are speculative and unproven. If the quality of gene patents remains a problem, stricter utility standards requiring more concrete uses may be called for. However, any lingering quality issues surrounding how gene inventions are examined could very well be impacted by the recent *KSR v. Teleflex* decision.

Still others fear that gene patents will be used to hinder research. They argue that if patent thickets were to form, it could become too costly or too troublesome for researchers to license the patented inventions they need, forcing them to abandon their research. There is anecdotal information that supports this notion that researchers have discontinued research pursuits because of the threat of lawsuits by gene patent holders. However, there is also data that suggests just the opposite; that gene patents have had little impact on basic research.

A recent survey by the National Academy of Sciences found that in biomedical research, there is a "lack of substantial evidence for a patent thicket or a patent blocking problem" primarily because researchers aren't very concerned about patents being enforced against them. However, the report went on to say that this nonchalant attitude was based on the assumption by many researchers that they qualify for a robust research use exception, which many believe was eliminated in the 2002 *Madey v. Duke* decision. Regardless, it might only take one major victory against a university to create a real and substantial chilling effect. As such, we may need to examine the effects or necessity of a clear research use exception.

Finally, for some, opposition to gene patents is a matter of principle. They point out that patents on genetic tests is harming patient access to, and stunting improvements of, these tests. First, it is reasoned that since most insurance providers do not provide coverage for genetic tests, the patent mark-up can price tests out of reach for many patients. In addition, some claim that gene patents have been asserted in order to prevent others from improving possibly inaccurate genetic tests and identifying whether the tests are even applicable to certain population subgroups. While I firmly support a patent holder's right to charge what the market will bare for his invention, using a patent to block efforts that check the efficacy of such tests borders on the realm of patent misuse and may constitute anti-competitive practices.

Patents are meant to encourage technical progress—thus, it is antithetical to the patent system for companies to use their patents to freeze a technology at a particular stage of development. But is that what is happening? Are the practices of a few unfairly coloring all gene patents in a negative light? Are complaints related to gene patents based more on how they are being used instead of what is being patented? We need to examine the role gene patents play in stimulating or stifling research and genetic testing. It is my hope that this hearing will help us answer these and many other underlying questions.

Mr. COBLE. Thank you, Mr. Chairman and ladies and gentlemen.

This is a good hearing topic, Mr. Chairman, in large part because the subject matter lends itself oftentimes to misrepresentation.

At the outset, it seems to me that an inventor whose application satisfies the requirements for gene patent is not trying to patent "life" or personal DNA chemistry in violation of the 13th amendment. The inventor's ultimate goal is to develop a protein-based drug, a diagnostic test, or a therapeutic modality that will improve public health, if not save lives.

I, therefore, hope the Subcommittee will collectively acknowledge after this hearing that gene patenting is a legitimate part of our patent system. It is a thriving component, it seems to me, of our knowledge-based economy. More importantly, gene patents ultimately contribute to the health and welfare of the American people and patients all over the world.

The National Institutes of Health is the world's largest agency for conducting basic medical and biological research with a budget in excess of $28 billion, but the pharmaceutical and biotech industries devote more than $50 billion annually to research. The process of identifying a DNA sequence through clinical testing and manufacturing of an FDA-approved drug may cost the patent holder in excess of a billion dollars, yet only a third of all drugs ever generate revenues sufficient to cover those costs, and the great majority, I am told, Mr. Chairman, of the biotech companies do not realize a profit.

Mr. Chairman, you did a very good, masterful job, I will say, in negotiating the recently passed Patent Reform Act of 2007, but one thing we learned while debating that legislation is that different industries employ different business models. They use the patent system in various and sundry ways.

American biotech companies are more reliant on the Patent Act than any other industry. While a few biotech companies are large, most are smaller and lack the internal financing resources to subsidize their drug research and development. This is especially true of small start-up companies whose valuation is an exclusive function of their patent portfolios.

At our hearing today, the witnesses and the Subcommittee will explore some legitimate topics associated with gene patents. Are gene patents an impediment to university research? Do they inhibit competition and limit patient access to diagnostic testing? Should the Government exercise march-in rights to promote greater testing and research?

I look forward to the testimonies of our witnesses today on these and other issues.

And, in conclusion, Mr. Chairman, on March the 14 of 2000, about 4 months before you and I were involved in a Subcommittee on this very issue, at a hearing—gene patents, as you know, make inventions—I remember President Clinton and Prime Minster Blair issued a joint statement on the human genome. They said that all genes in the human body should be made freely available to scientists everywhere, and some interpreted that as an announcement of new Government policy that genes could not be patented.

Then the biotech industry, of course, experienced bad difficulty, losing several billion dollars and, the following day, the White House released another statement emphasizing that the Administration supported the patenting of genes.

I guess the moral of the story, Mr. Chairman, is to proceed cautiously and deliberately, and you have a good reputation of doing that, and I think I do, too.

This is a good topic for an oversight hearing, but I think we must exercise great care about legislating in this area, lest possibly important industry and compromised public health could result.

Thank you, Mr. Chairman.

[The prepared statement of Mr. Coble follows:]

PREPARED STATEMENT OF THE HONORABLE HOWARD COBLE, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NORTH CAROLINA, AND RANKING MEMBER, SUBCOMMITTEE ON COURTS, THE INTERNET, AND INTELLECTUAL PROPERTY

Thank you, Mr. Chairman.

This is a good hearing topic, in large part because the subject matter lends itself to misrepresentation. At the outset, let's be clear that an inventor whose application satisfies the requirements for a gene patent isn't trying to patent "life" or personal DNA chemistry in violation of the 13th Amendment. The inventor's ultimate goal is to develop a protein-based drug, a diagnostic test, or a therapeutic modality that will improve public health if not save lives.

I therefore hope the Subcommittee will collectively acknowledge after this hearing that gene patenting is a legitimate part of our patent system. It is a thriving component of our knowledge-based economy. More importantly, gene patents ultimately contribute to the health and welfare of the American people and patients all over the world.

The National Institutes of Health is the world's largest agency for conducting basic medical and biological research, with a budget in excess of $28 billion. But the pharmaceutical and biotech industries devote more than $50 billion annually to research. The process of identifying a DNA sequence through clinical testing and manufacturing of an FDA-approved drug may cost the patent holder north of one-billion dollars. Yet only a third of all drugs ever generate revenue sufficient to cover their costs. And the great majority of biotech companies do not turn a profit.

Mr. Chairman, you did an outstanding job of negotiating House passage of the "Patent Reform Act of 2007." One thing we learned while debating the legislation is that different industries employ different business models that use the patent system in different ways. American biotech companies are more reliant on the Patent Act than any other industry. While a few biotech companies are large, most are much smaller and lack the internal financing resources to subsidize their drug research and development. This is especially true of small start-up companies, whose valuation is an exclusive function of their patent portfolios.

At our hearing today, the witnesses and the Subcommittee will explore some legitimate topics associated with gene patents. Are gene patents an impediment to university research? Do they inhibit competition and limit patient access to diagnostic testing? Should the government exercise "march-in" rights to promote greater testing and research? I look forward to the testimony of our witnesses today on these and other issues.

But I conclude with a cautionary tale. On March 14, 2000, about four months before I chaired a Subcommittee hearing on gene patents and genomic inventions, President Clinton and Prime Minister Blair issued a joint statement on the human genome. They said that all genes in the human body "should be made freely available to scientists everywhere," implying the announcement of a new government policy that genes could not be patented. The biotech industry promptly crashed, losing more than $40 billion in market capitalization. The following day the White House released another statement emphasizing that the Administration supported the patenting of genes.

The moral of the story, Mr. Chairman, is to proceed cautiously and deliberately. This is a good topic for an oversight hearing. But we must exercise great care about legislating in this area, lest we wreck an important industry and compromise public health.

That concludes my statement, Mr. Chairman.

Mr. BERMAN. Thank you, Mr. Coble.

I am wondering whether the asset value of the companies went back up by $2 billion on that next day when he said that because, if it had, I can say anything now and correct it tomorrow.

Mr. COBLE. And I am not sure I can answer that. [Laughter.]

Mr. BERMAN. I now will introduce a very distinguished panel of witnesses.

Lawrence Sung is Director of the Intellectual Property law program at the University of Maryland School of Law. He is a partner in the Washington, D.C., office of Dewey & LeBouef, where he specializes in biotechnology, medical device, and pharmaceutical patent litigation and counseling. Additionally, he serves as a consultant to the National Human Genome Research Institute and as Chair for Intellectual Property for the National Research Council. Professor Sung earned a Ph.D. in microbiology from the U.S. Department of Defense Uniformed Services University of the Health Sciences and a J.D. from American University's Washington College of Law.

John Soderstrom is the Managing Director of the Office of Cooperative Research at Yale University, where he is responsible for managing the university's intellectual property portfolio, executing commercialization strategies and developing spinoff ventures. His posture has allowed him to participate in the formation of more than 25 new start-up companies, many in the biotechnology sector. Prior to joining Yale, Dr. Soderstrom was the director of program development for Oak Ridge National Laboratory. Dr. Soderstrom is also President-Elect of the Association of University Technology Managers. Dr. Soderstrom received his Ph.D. from Northwestern University.

And I might point out we have had no less than the President of Yale University testifying on patent issues several times in the past few years.

Marc Grodman is founder of Bio-Reference Laboratories, the largest clinical laboratory operating in the Northeast. In addition to being a major regional laboratory, Bio-Reference Laboratories also provides national services in informatics and genomics. Dr. Grodman is also an Assistant Professor of clinical medicine at Columbia University's College of Physicians and Surgeons. Dr. Grodman received his B.A. from the University of Pennsylvania, his M.D. from Columbia University, and attended Harvard University's Kennedy School of Government.

Jeffrey Kushan is a Partner with Sidley & Austin, where he serves as Practice Group Chair for the firm's D.C. office. Mr. Kushan focuses his practice on Hatch-Waxman patent litigation, patent appeals and proceedings, patent portfolio reviews, and he represents clients, including trade associations, on domestic and international patent policy matters. He is testifying today on behalf of the Biotechnology Industry Organization. Before entering private practice, Mr. Kushan worked in Government as a patent examiner, in various policy advisory positions at the USPTO, and as an IP negotiator at the USTR. Mr. Kushan received his M.A. in chemistry from the University of North Carolina at Chapel Hill and his J.D. from George Washington University.

Gentlemen, it is really an honor to have you all here today. Your written statements will be made part of the record, in their entirety. I would ask you, if you would be willing to, to summarize your testimony in 5 minutes or less, and to stay within the time, there is a timing light at the table. When 1 minute remains, the light will switch from green to yellow, and then red when then 5 minutes are up.

We are glad to have you here.

Dr. Sung?

TESTIMONY OF LAWRENCE M. SUNG, J.D., Ph.D., LAW SCHOOL PROFESSOR AND INTELLECTUAL PROPERTY LAW PROGRAM DIRECTOR, UNIVERSITY OF MARYLAND, SCHOOL OF LAW, BALTIMORE, MD

Mr. SUNG. My charge during our brief time is relatively modest. I am not here to represent an organization, nor am I here to press an agenda. Rather, I hope to help inform your deliberations on gene patenting with insights about the nature of patent protections for genomic inventions and also to describe some available options that might assist in effectuating the particular balance between patent exclusivity and public access you ultimately deem appropriate.

These may not be actual answers to the question of gene patenting, but then, as you know, what law professors do best is to answer a question by raising more questions.

This Subcommittee has had the benefit of hearings focusing on the state of the patent system and on the possibility of patent reform legislation. I will not revisit these general principles of the patent system, but instead address some of the distinctions of gene patenting, three in particular.

First, patenting genomic inventions is different because the underlying technology is different. Metaphorically speaking, in the physical sciences, if one dedicates her career to climbing the highest mountain, then on that day she can be confident that she has seen all there is to see. By contrast in the biological sciences, once you summit the highest mountain, only then do you see that there are other mountains you have never seen before. The science in this field is fluid, and this creates an inherent tension with the patent system which, like other systems of legal rights, depends upon static definition. Gene patents defy this type of containment.

Second, genes are simply something that we have a sense should be part of the public common. That the subject matter might fit within the legal standards of what is patentable does not necessarily change the fact that many are left feeling that something is just not right about treating genetic information as property.

Third, the temporal distortion that exists between the time one files a patent application and the time the courts adjudicate those patent rights seems even greater when dealing with gene patents. Sometimes decades separate these two events, and when courts make pronouncements today about what was a fledgling technology 20 years ago, that does not sit well with a public that sees foremost what is at stake today.

Now the state of gene patenting has seen significant evolution. When technology developed to allow rapid gene sequencing to occur, patent claims began being filed in hordes, what some called the patent gold rush, but, like most gold rushes, virtually all of the claims were speculative and the prospect of great wealth became illusory.

The Patent Office wisely issued a moratorium on examination until setting forth revised standards of utility in written description that could be applied more sensibly to patent claims to DNA fragments known as expressed sequence tags or ESTs. This era concluded with the 2005 Federal Circuit decision In re Fisher which clarified that DNA fragments without some demonstrated knowledge about its biological relevance were not patentable for failure to teach a specific substantial and credible utility.

This case arguably alleviates much of the wild concern over what many generically and inaccurately call gene patents. To be clear, gene patents still exist, but they are claims for DNA for which we have been taught both what it is and what it does, and this is somewhat more acceptable than the EST patent claims that the public first rallied against.

But the issue of gene patents and their effect on research and public access to genetic testing remains. For those of the mind that action is necessary, one option is the maintenance or the enhancement of the rigor with which the Patent Office examines gene patent applications. The evolving jurisprudence generally in the patent law doctrines of anticipation, inherency, and obviousness, including the Supreme Court's decision in *KSR v. Teleflex*, combined with the existing disclosure requirements of written description and enablement suggest that fewer gene patents will pass muster.

In addition, the Supreme Court decision in *Merck v. Integra* will likely lessen the ability of certain patents, including some gene patents to be enforced. The Supreme Court decision in *eBay v.*

MercExchange also implicates the restraint on the grounds of public interest in granting injunctive relief to gene patent plaintiffs even where infringement has occurred.

The Government's implementation of existing march-in rights for federally funded technology covered by gene patents would be another avenue to ensure public access.

For those that feel the status quo or the reinvigoration of these standards fall short, new legislation might be considered and these include three options. First is the creation of the heightened standard of inventorship that effectively precludes the mere elucidation of a natural property, such as the DNA sequence or a biological pathway. Second is compulsory licensing of gene patents or some form of mandatory patent pooling of gene patents. And, third, is an academic research use exemption from patent infringement.

In this last regard, my written submission for this hearing details a proposal of an elective right to use patented technology.

I appreciate your attention. In closing, I ask your indulgence to be mindful that in the brief time here, I have necessarily oversimplified many aspects of a complex set of considerations. As I caution in my written statement, generalization is problematic with regard to gene patents, and I hope you will seek further insights of others on the important specifics.

Thank you.

[The prepared statement of Mr. Sung follows:]

PREPARED STATEMENT OF LAWRENCE M. SUNG

Testimony Before the House Judiciary Subcommittee on Courts, the Internet, and Intellectual Property

30 October 2007 Hearing on
Stifling or Stimulating –
The Role of Gene Patents in Research and Genetic Testing

Statement of
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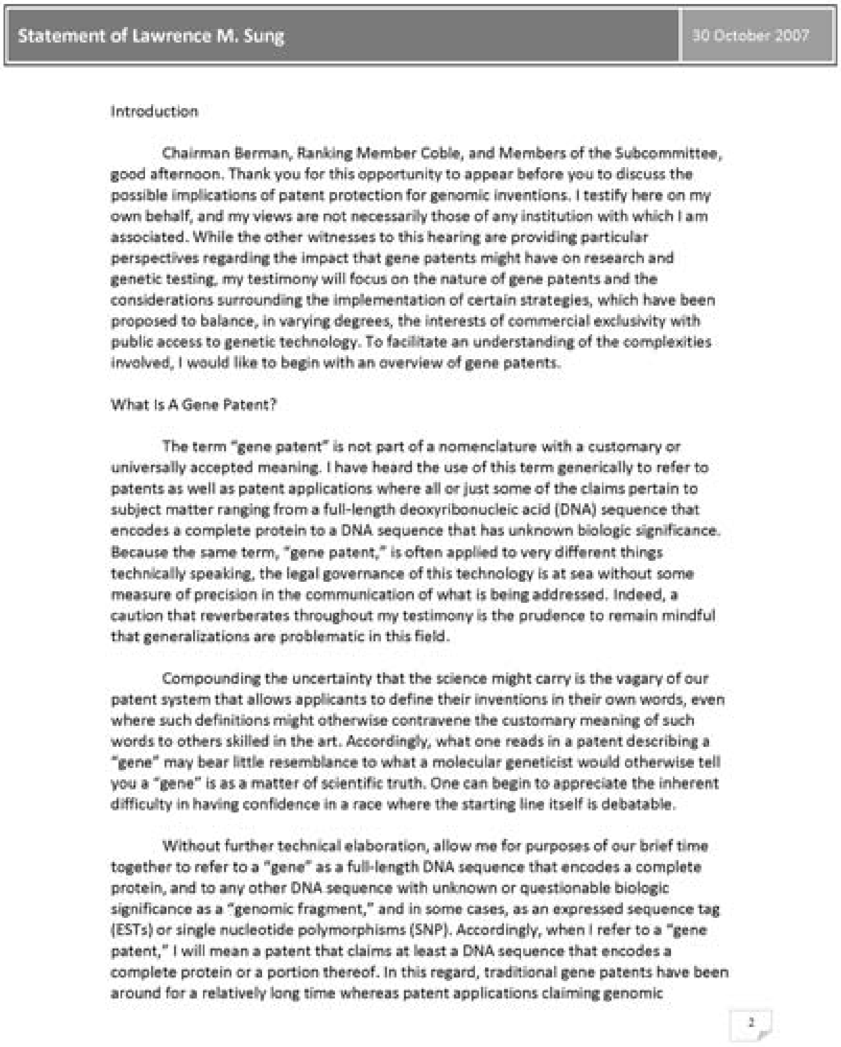


Statement of Lawrence M. Sung

30 October 2007

Introduction

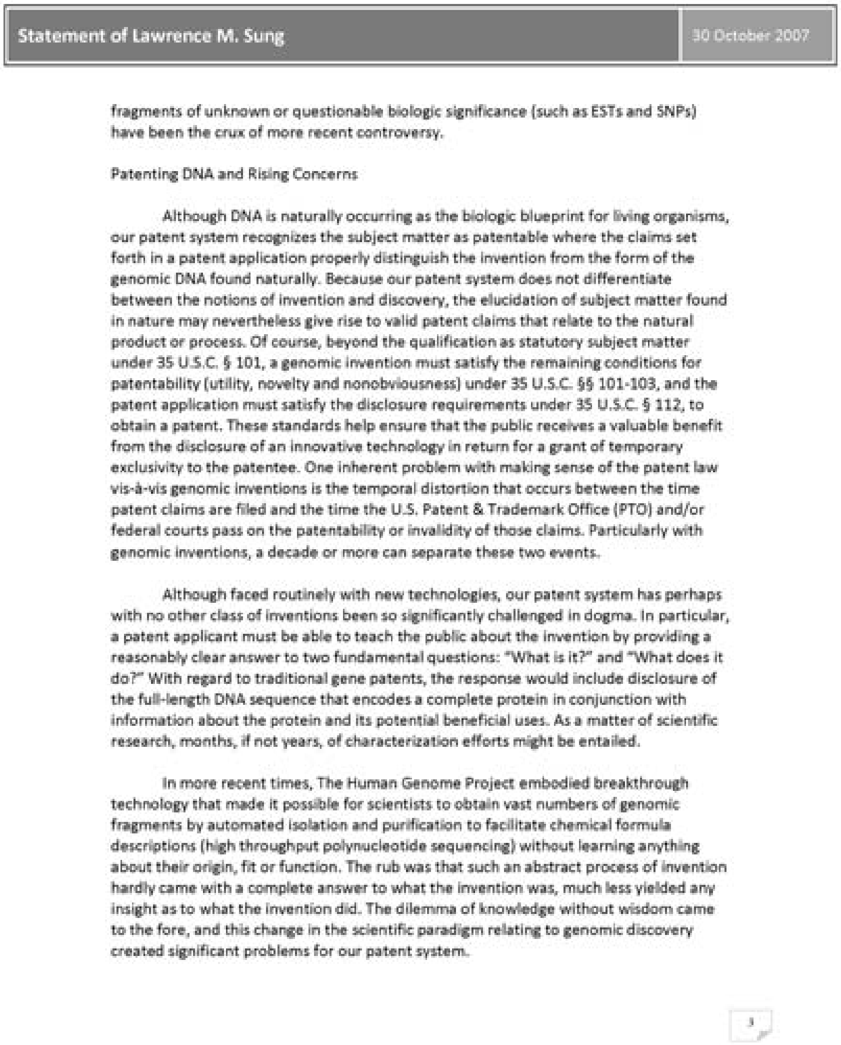
Chairman Berman, Ranking Member Coble, and Members of the Subcommittee, good afternoon. Thank you for this opportunity to appear before you to discuss the possible implications of patent protection for genomic inventions. I testify here on my own behalf, and my views are not necessarily those of any institution with which I am associated. While the other witnesses to this hearing are providing particular perspectives regarding the impact that gene patents might have on research and genetic testing, my testimony will focus on the nature of gene patents and the considerations surrounding the implementation of certain strategies, which have been proposed to balance, in varying degrees, the interests of commercial exclusivity with public access to genetic technology. To facilitate an understanding of the complexities involved, I would like to begin with an overview of gene patents.

What Is A Gene Patent?

The term "gene patent" is not part of a nomenclature with a customary or universally accepted meaning. I have heard the use of this term generically to refer to patents as well as patent applications where all or just some of the claims pertain to subject matter ranging from a full-length deoxyribonucleic acid (DNA) sequence that encodes a complete protein to a DNA sequence that has unknown biologic significance. Because the same term, "gene patent," is often applied to very different things technically speaking, the legal governance of this technology is at sea without some measure of precision in the communication of what is being addressed. Indeed, a caution that reverberates throughout my testimony is the prudence to remain mindful that generalizations are problematic in this field.

Compounding the uncertainty that the science might carry is the vagary of our patent system that allows applicants to define their inventions in their own words, even where such definitions might otherwise contravene the customary meaning of such words to others skilled in the art. Accordingly, what one reads in a patent describing a "gene" may bear little resemblance to what a molecular geneticist would otherwise tell you a "gene" is as a matter of scientific truth. One can begin to appreciate the inherent difficulty in having confidence in a race where the starting line itself is debatable.

Without further technical elaboration, allow me for purposes of our brief time together to refer to a "gene" as a full-length DNA sequence that encodes a complete protein, and to any other DNA sequence with unknown or questionable biologic significance as a "genomic fragment," and in some cases, as an expressed sequence tag (ESTs) or single nucleotide polymorphisms (SNP). Accordingly, when I refer to a "gene patent," I will mean a patent that claims at least a DNA sequence that encodes a complete protein or a portion thereof. In this regard, traditional gene patents have been around for a relatively long time whereas patent applications claiming genomic



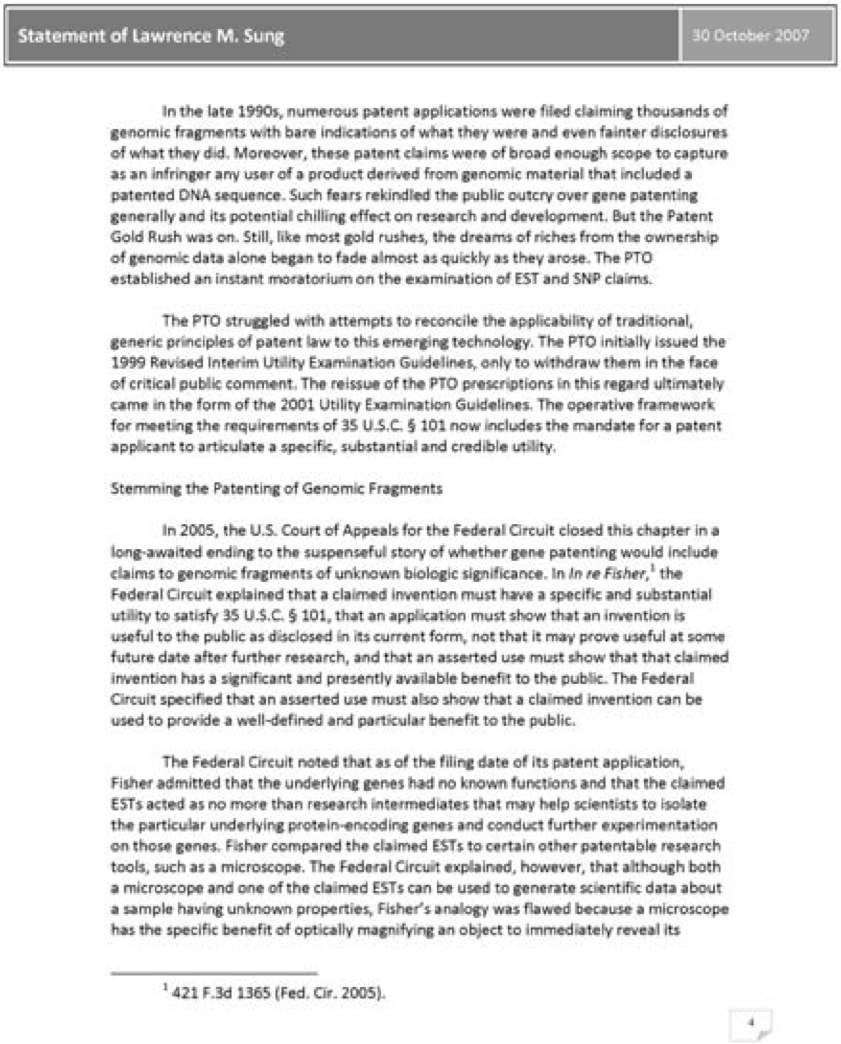
fragments of unknown or questionable biologic significance (such as ESTs and SNPs) have been the crux of more recent controversy.

Patenting DNA and Rising Concerns

Although DNA is naturally occurring as the biologic blueprint for living organisms, our patent system recognizes the subject matter as patentable where the claims set forth in a patent application properly distinguish the invention from the form of the genomic DNA found naturally. Because our patent system does not differentiate between the notions of invention and discovery, the elucidation of subject matter found in nature may nevertheless give rise to valid patent claims that relate to the natural product or process. Of course, beyond the qualification as statutory subject matter under 35 U.S.C. § 101, a genomic invention must satisfy the remaining conditions for patentability (utility, novelty and nonobviousness) under 35 U.S.C. §§ 101-103, and the patent application must satisfy the disclosure requirements under 35 U.S.C. § 112, to obtain a patent. These standards help ensure that the public receives a valuable benefit from the disclosure of an innovative technology in return for a grant of temporary exclusivity to the patentee. One inherent problem with making sense of the patent law vis-à-vis genomic inventions is the temporal distortion that occurs between the time patent claims are filed and the time the U.S. Patent & Trademark Office (PTO) and/or federal courts pass on the patentability or invalidity of those claims. Particularly with genomic inventions, a decade or more can separate these two events.

Although faced routinely with new technologies, our patent system has perhaps with no other class of inventions been so significantly challenged in dogma. In particular, a patent applicant must be able to teach the public about the invention by providing a reasonably clear answer to two fundamental questions: "What is it?" and "What does it do?" With regard to traditional gene patents, the response would include disclosure of the full-length DNA sequence that encodes a complete protein in conjunction with information about the protein and its potential beneficial uses. As a matter of scientific research, months, if not years, of characterization efforts might be entailed.

In more recent times, The Human Genome Project embodied breakthrough technology that made it possible for scientists to obtain vast numbers of genomic fragments by automated isolation and purification to facilitate chemical formula descriptions (high throughput polynucleotide sequencing) without learning anything about their origin, fit or function. The rub was that such an abstract process of invention hardly came with a complete answer to what the invention was, much less yielded any insight as to what the invention did. The dilemma of knowledge without wisdom came to the fore, and this change in the scientific paradigm relating to genomic discovery created significant problems for our patent system.



In the late 1990s, numerous patent applications were filed claiming thousands of genomic fragments with bare indications of what they were and even fainter disclosures of what they did. Moreover, these patent claims were of broad enough scope to capture as an infringer any user of a product derived from genomic material that included a patented DNA sequence. Such fears rekindled the public outcry over gene patenting generally and its potential chilling effect on research and development. But the Patent Gold Rush was on. Still, like most gold rushes, the dreams of riches from the ownership of genomic data alone began to fade almost as quickly as they arose. The PTO established an instant moratorium on the examination of EST and SNP claims.

The PTO struggled with attempts to reconcile the applicability of traditional, generic principles of patent law to this emerging technology. The PTO initially issued the 1999 Revised Interim Utility Examination Guidelines, only to withdraw them in the face of critical public comment. The reissue of the PTO prescriptions in this regard ultimately came in the form of the 2001 Utility Examination Guidelines. The operative framework for meeting the requirements of 35 U.S.C. § 101 now includes the mandate for a patent applicant to articulate a specific, substantial and credible utility.

Stemming the Patenting of Genomic Fragments

In 2005, the U.S. Court of Appeals for the Federal Circuit closed this chapter in a long-awaited ending to the suspenseful story of whether gene patenting would include claims to genomic fragments of unknown biologic significance. In *In re Fisher*,[1] the Federal Circuit explained that a claimed invention must have a specific and substantial utility to satisfy 35 U.S.C. § 101, that an application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research, and that an asserted use must show that that claimed invention has a significant and presently available benefit to the public. The Federal Circuit specified that an asserted use must also show that a claimed invention can be used to provide a well-defined and particular benefit to the public.

The Federal Circuit noted that as of the filing date of its patent application, Fisher admitted that the underlying genes had no known functions and that the claimed ESTs acted as no more than research intermediates that may help scientists to isolate the particular underlying protein-encoding genes and conduct further experimentation on those genes. Fisher compared the claimed ESTs to certain other patentable research tools, such as a microscope. The Federal Circuit explained, however, that although both a microscope and one of the claimed ESTs can be used to generate scientific data about a sample having unknown properties, Fisher's analogy was flawed because a microscope has the specific benefit of optically magnifying an object to immediately reveal its

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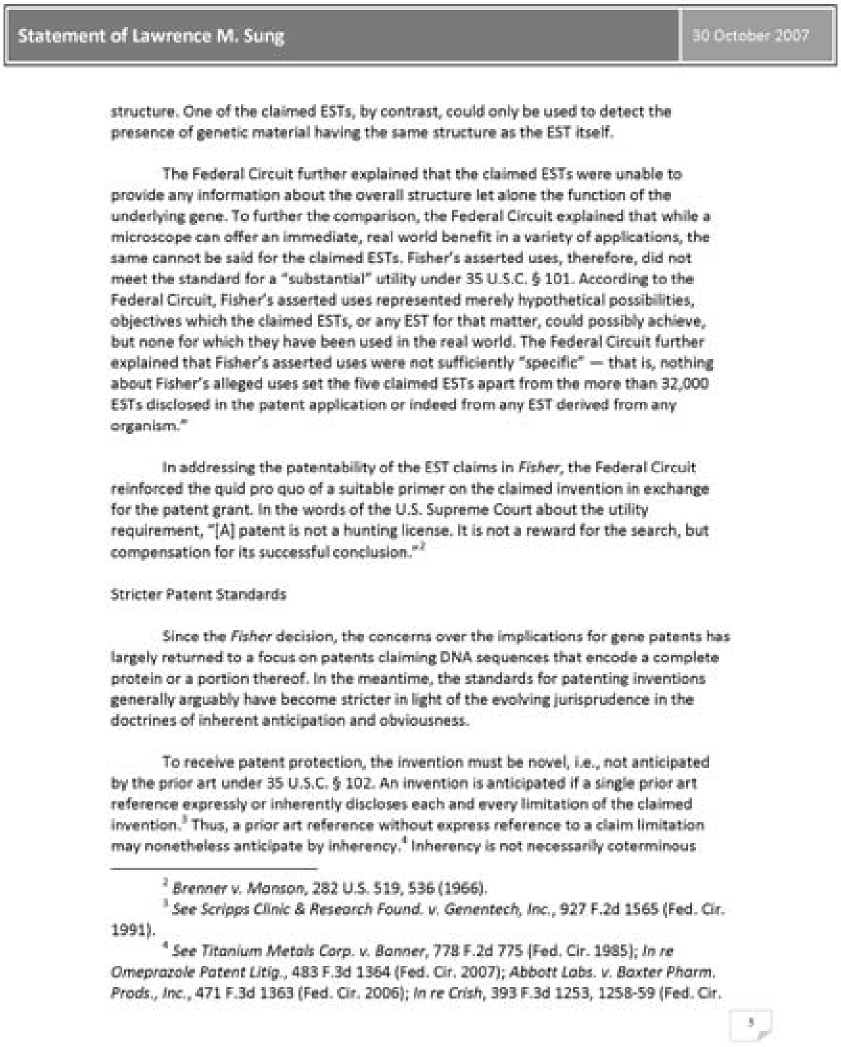
[1] 421 F.3d 1365 (Fed. Cir. 2005).



structure. One of the claimed ESTs, by contrast, could only be used to detect the presence of genetic material having the same structure as the EST itself.

The Federal Circuit further explained that the claimed ESTs were unable to provide any information about the overall structure let alone the function of the underlying gene. To further the comparison, the Federal Circuit explained that while a microscope can offer an immediate, real world benefit in a variety of applications, the same cannot be said for the claimed ESTs. Fisher's asserted uses, therefore, did not meet the standard for a "substantial" utility under 35 U.S.C. § 101. According to the Federal Circuit, Fisher's asserted uses represented merely hypothetical possibilities, objectives which the claimed ESTs, or any EST for that matter, could possibly achieve, but none for which they have been used in the real world. The Federal Circuit further explained that Fisher's asserted uses were not sufficiently "specific" — that is, nothing about Fisher's alleged uses set the five claimed ESTs apart from the more than 32,000 ESTs disclosed in the patent application or indeed from any EST derived from any organism."

In addressing the patentability of the EST claims in *Fisher*, the Federal Circuit reinforced the quid pro quo of a suitable primer on the claimed invention in exchange for the patent grant. In the words of the U.S. Supreme Court about the utility requirement, "[A] patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."[2]

Stricter Patent Standards

Since the *Fisher* decision, the concerns over the implications for gene patents has largely returned to a focus on patents claiming DNA sequences that encode a complete protein or a portion thereof. In the meantime, the standards for patenting inventions generally arguably have become stricter in light of the evolving jurisprudence in the doctrines of inherent anticipation and obviousness.

To receive patent protection, the invention must be novel, i.e., not anticipated by the prior art under 35 U.S.C. § 102. An invention is anticipated if a single prior art reference expressly or inherently discloses each and every limitation of the claimed invention.[3] Thus, a prior art reference without express reference to a claim limitation may nonetheless anticipate by inherency.[4] Inherency is not necessarily coterminous

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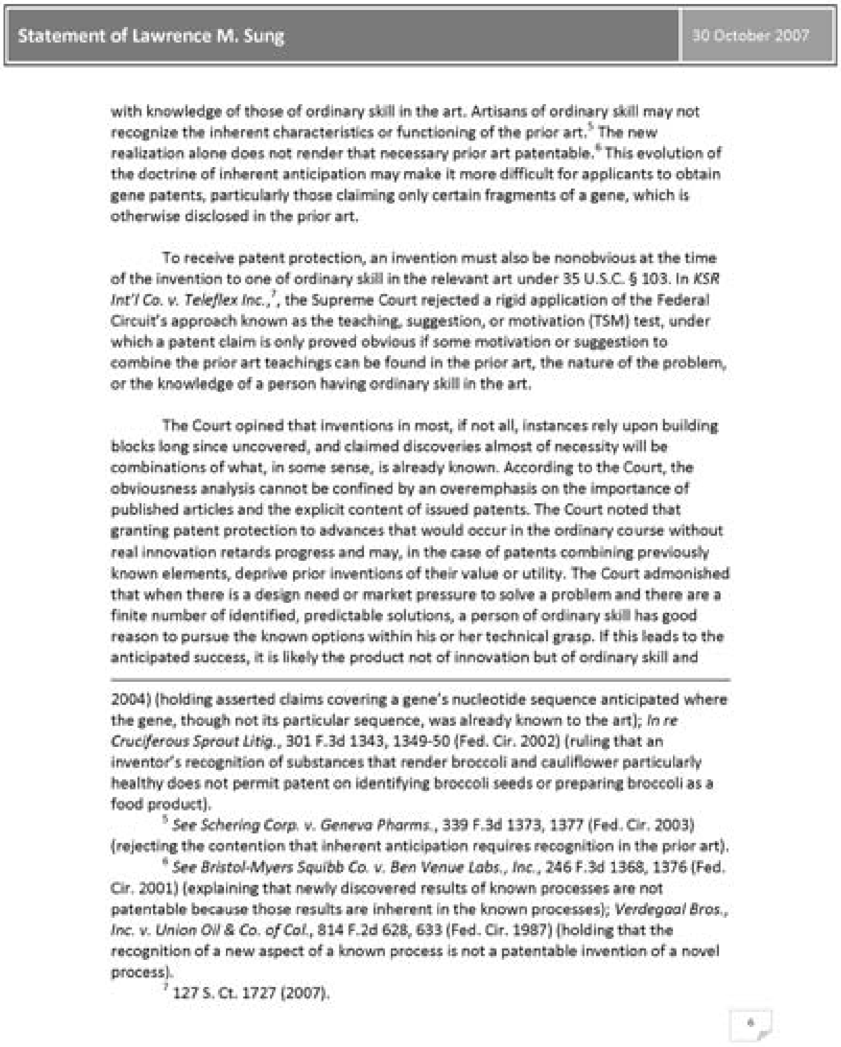
[2] *Brenner v. Manson*, 282 U.S. 519, 536 (1966).

[3] *See Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991).

[4] *See Titanium Metals Corp. v. Bonner*, 778 F.2d 775 (Fed. Cir. 1985); *In re Omeprazole Patent Litig.*, 483 F.3d 1364 (Fed. Cir. 2007); *Abbott Labs. v. Baxter Pharm. Prods., Inc.*, 471 F.3d 1363 (Fed. Cir. 2006); *In re Crish*, 393 F.3d 1253, 1258-59 (Fed. Cir.



with knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art.[5] The new realization alone does not render that necessary prior art patentable.[6] This evolution of the doctrine of inherent anticipation may make it more difficult for applicants to obtain gene patents, particularly those claiming only certain fragments of a gene, which is otherwise disclosed in the prior art.

To receive patent protection, an invention must also be nonobvious at the time of the invention to one of ordinary skill in the relevant art under 35 U.S.C. § 103. In *KSR Int'l Co. v. Teleflex Inc.*,[7], the Supreme Court rejected a rigid application of the Federal Circuit's approach known as the teaching, suggestion, or motivation (TSM) test, under which a patent claim is only proved obvious if some motivation or suggestion to combine the prior art teachings can be found in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art.

The Court opined that inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known. According to the Court, the obviousness analysis cannot be confined by an overemphasis on the importance of published articles and the explicit content of issued patents. The Court noted that granting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, in the case of patents combining previously known elements, deprive prior inventions of their value or utility. The Court admonished that when there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and

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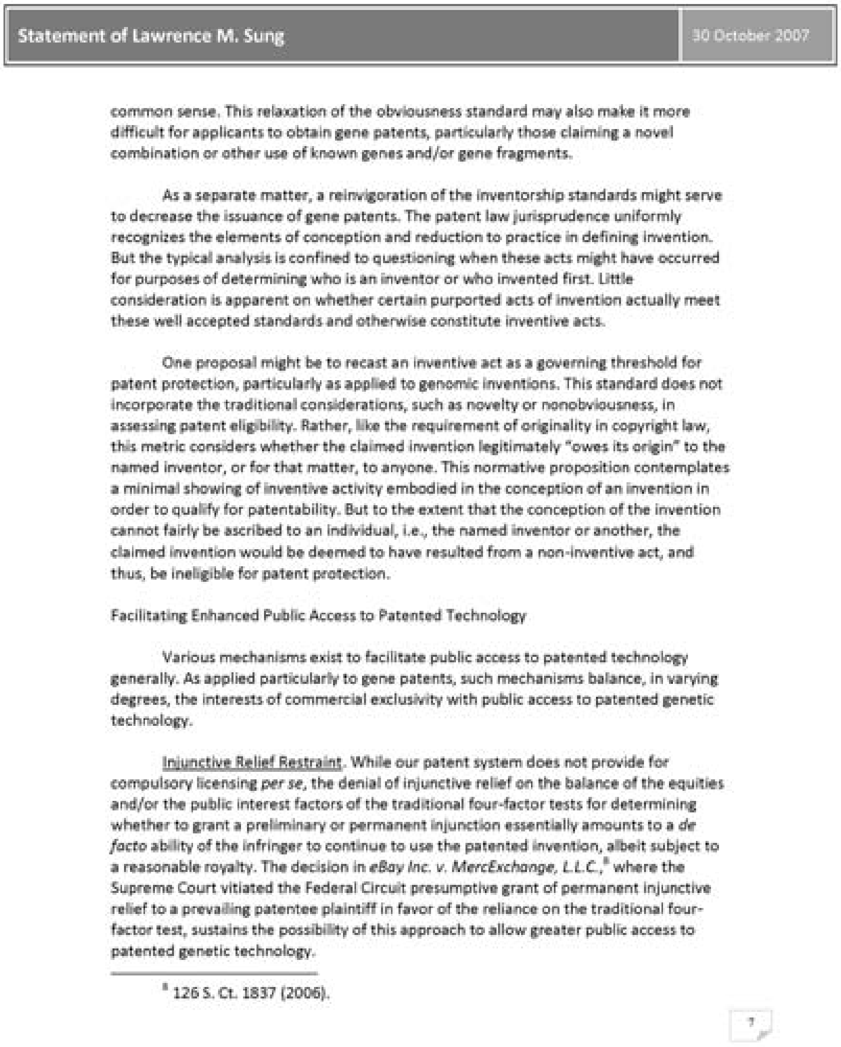
2004) (holding asserted claims covering a gene's nucleotide sequence anticipated where the gene, though not its particular sequence, was already known to the art); *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349-50 (Fed. Cir. 2002) (ruling that an inventor's recognition of substances that render broccoli and cauliflower particularly healthy does not permit patent on identifying broccoli seeds or preparing broccoli as a food product).

[5] *See Schering Corp. v. Geneva Pharms.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition in the prior art).

[6] *See Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1376 (Fed. Cir. 2001) (explaining that newly discovered results of known processes are not patentable because those results are inherent in the known processes); *Verdegaal Bros., Inc. v. Union Oil & Co. of Cal.*, 814 F.2d 628, 633 (Fed. Cir. 1987) (holding that the recognition of a new aspect of a known process is not a patentable invention of a novel process).

[7] 127 S. Ct. 1727 (2007).



common sense. This relaxation of the obviousness standard may also make it more difficult for applicants to obtain gene patents, particularly those claiming a novel combination or other use of known genes and/or gene fragments.

As a separate matter, a reinvigoration of the inventorship standards might serve to decrease the issuance of gene patents. The patent law jurisprudence uniformly recognizes the elements of conception and reduction to practice in defining invention. But the typical analysis is confined to questioning when these acts might have occurred for purposes of determining who is an inventor or who invented first. Little consideration is apparent on whether certain purported acts of invention actually meet these well accepted standards and otherwise constitute inventive acts.

One proposal might be to recast an inventive act as a governing threshold for patent protection, particularly as applied to genomic inventions. This standard does not incorporate the traditional considerations, such as novelty or nonobviousness, in assessing patent eligibility. Rather, like the requirement of originality in copyright law, this metric considers whether the claimed invention legitimately "owes its origin" to the named inventor, or for that matter, to anyone. This normative proposition contemplates a minimal showing of inventive activity embodied in the conception of an invention in order to qualify for patentability. But to the extent that the conception of the invention cannot fairly be ascribed to an individual, i.e., the named inventor or another, the claimed invention would be deemed to have resulted from a non-inventive act, and thus, be ineligible for patent protection.

Facilitating Enhanced Public Access to Patented Technology

Various mechanisms exist to facilitate public access to patented technology generally. As applied particularly to gene patents, such mechanisms balance, in varying degrees, the interests of commercial exclusivity with public access to patented genetic technology.

Injunctive Relief Restraint. While our patent system does not provide for compulsory licensing *per se*, the denial of injunctive relief on the balance of the equities and/or the public interest factors of the traditional four-factor tests for determining whether to grant a preliminary or permanent injunction essentially amounts to a *de facto* ability of the infringer to continue to use the patented invention, albeit subject to a reasonable royalty. The decision in *eBay Inc. v. MercExchange, L.L.C.*,[8] where the Supreme Court vitiated the Federal Circuit presumptive grant of permanent injunctive relief to a prevailing patentee plaintiff in favor of the reliance on the traditional four-factor test, sustains the possibility of this approach to allow greater public access to patented genetic technology.

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[8] 126 S. Ct. 1837 (2006).

Patent Pools. For a biotechnology company, there is arguably no greater asset than a proprietary position on genetic data that might become the platform for the development of commercially significant biological products. Besides its straightforward function as a direct template for such biologics, genomic data also has enormous potential as a basic research tool with many possible applications. The technical leap from knowledge of mere DNA sequence to such downstream applications, however, while perhaps grounded in accepted scientific methods, is certainly not trivial. Accordingly, the dependency of the biotechnology industry on patent exclusivity remains robust. Matching this are the continuing concerns over patent thickets and other obstacles to access and development.

As the biotechnology industry has matured, the embrace of cooperative market-based technology transfer strategies similar to those relied upon in other technology sectors is perhaps within reach. In 1998, I suggested that the interplay between historical experiences and future prospects in biotechnology made patent pooling arrangements a ripe consideration for the industry, and that the patent landscape should not be allowed to preclude the realization of financial rewards associated with the complex research efforts of biotechnology companies to understand and to harness the biological processes involved.[9]

At its core, biotechnology is the exploitation of nature's design, standing on the shoulders of the biological templates of DNA and ribonucleic acid (RNA). For biotechnology, genetic information represents an "industry standard" analogous to those described above in the electronics and telecommunications areas. Accordingly, the landscape of increasing patent protection to this genetic material favors the voluntary entry of biotechnology industry members into patent pooling arrangements.

Indeed, the vast amount of genetic information, and its significance as a fundamental research tool even absent functional knowledge, can give rise to an almost overwhelming number of patents, the true value of which may be unascertainable

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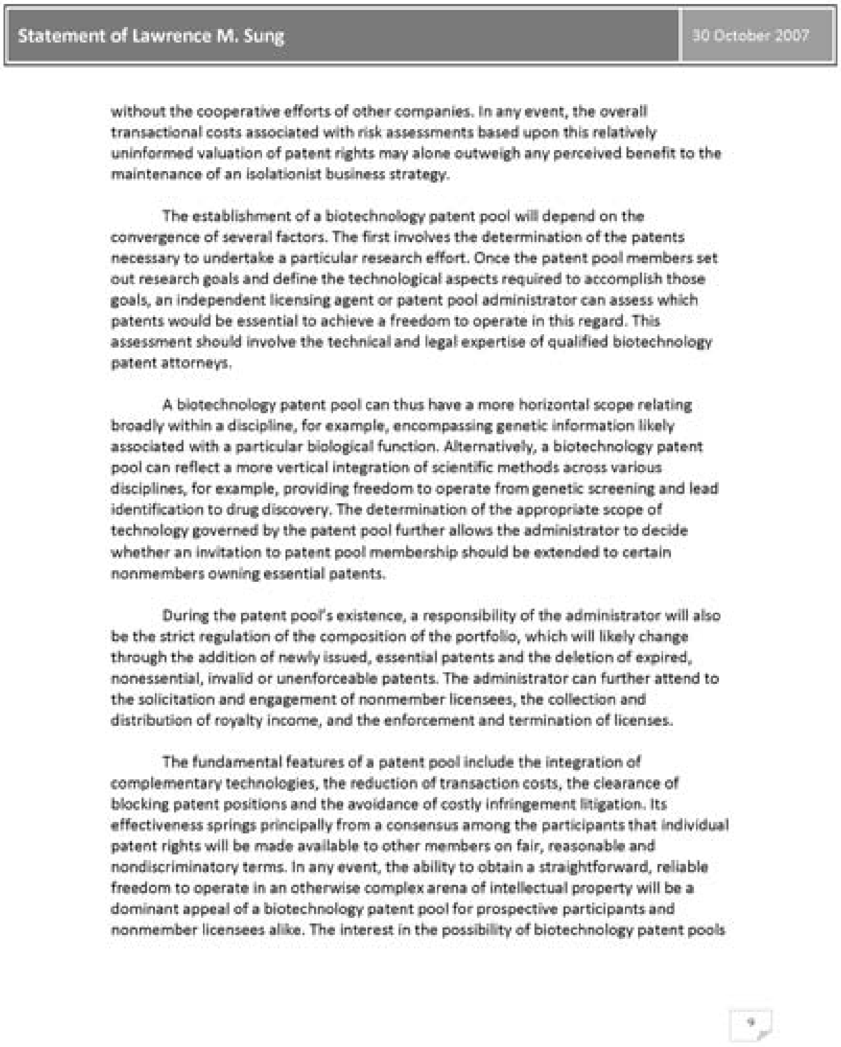
[9] Lawrence M. Sung *et al.*, *Greater Predictability May Result in Patent Pools As the Federal Circuit Refines Scope of Biotech Claims, Use of Collective Rights Becomes Likely*, Nat'l L.J. (Jun. 22, 1998), cited in USPTO White Paper, *Patent Pools: A Solution to the Problem of Access in Biotechnology Patents?* (Dec. 5, 2000). In 2002, I testified, during part of the Joint U.S. Department of Justice and Federal Trade Commission hearings on Competition and Intellectual Property Law and Policy in the Knowledge-Based Economy, that given the dynamics of biotechnology research and development, the reliance by the industry on cooperative market-based technology transfer strategies through patent pools or other collective rights organizations may be inevitable. Lawrence M. Sung, Patent Pools and Cross-Licensing: When Do They Promote or Harm Competition? (Apr. 17, 2002).



without the cooperative efforts of other companies. In any event, the overall transactional costs associated with risk assessments based upon this relatively uninformed valuation of patent rights may alone outweigh any perceived benefit to the maintenance of an isolationist business strategy.

The establishment of a biotechnology patent pool will depend on the convergence of several factors. The first involves the determination of the patents necessary to undertake a particular research effort. Once the patent pool members set out research goals and define the technological aspects required to accomplish those goals, an independent licensing agent or patent pool administrator can assess which patents would be essential to achieve a freedom to operate in this regard. This assessment should involve the technical and legal expertise of qualified biotechnology patent attorneys.

A biotechnology patent pool can thus have a more horizontal scope relating broadly within a discipline, for example, encompassing genetic information likely associated with a particular biological function. Alternatively, a biotechnology patent pool can reflect a more vertical integration of scientific methods across various disciplines, for example, providing freedom to operate from genetic screening and lead identification to drug discovery. The determination of the appropriate scope of technology governed by the patent pool further allows the administrator to decide whether an invitation to patent pool membership should be extended to certain nonmembers owning essential patents.

During the patent pool's existence, a responsibility of the administrator will also be the strict regulation of the composition of the portfolio, which will likely change through the addition of newly issued, essential patents and the deletion of expired, nonessential, invalid or unenforceable patents. The administrator can further attend to the solicitation and engagement of nonmember licensees, the collection and distribution of royalty income, and the enforcement and termination of licenses.

The fundamental features of a patent pool include the integration of complementary technologies, the reduction of transaction costs, the clearance of blocking patent positions and the avoidance of costly infringement litigation. Its effectiveness springs principally from a consensus among the participants that individual patent rights will be made available to other members on fair, reasonable and nondiscriminatory terms. In any event, the ability to obtain a straightforward, reliable freedom to operate in an otherwise complex arena of intellectual property will be a dominant appeal of a biotechnology patent pool for prospective participants and nonmember licensees alike. The interest in the possibility of biotechnology patent pools as mechanisms to balance the interests of commercial exclusivity with public access to patented genetic technology has resurged in recent years.[10]

March-In Rights. Under 35 U.S.C. § 203 (codifying a portion of the Bayh-Dole Act), the federal government retains "march-in rights" for government funded inventions owned by small businesses or nonprofit organizations. In situations of nonexploitation of the invention or public health threat, the funding agency may request the patentee or exclusive licensee to grant an appropriate license to another. If the request is refused, the funding agency may grant its own license, without restriction, including a license grant to a direct competitor. While the federal government historically has never exercised such rights, this entitlement has arguably greater implications for government funded genomic inventions, presumably because of the heightened relevance of the subject matter to potential public health and bioterrorism concerns.

Clinical Trial Exemption. At present, the only statutory exemption to patent infringement liability exists with 35 U.S.C. § 271(e)(1), which is limited to activity reasonably related to the preparation and submission of an application for federal regulatory approval. Such activity may include experimentation and other data gathering. In this regard, § 271(e)(1) can be fairly characterized as an experimental or research use defense applicable only in the specific context of regulatory compliance.

While § 271(e)(1) exempts from infringement such activity by the generic drug manufacturer that would otherwise infringe § 271(a), so long as that activity is reasonably related to the FDA application, § 271(e)(2) provides a cause of action for infringement based upon the filing of an application to the Food and Drug Administration (FDA) for market approval of a generic drug. The statutory scheme thus balances the interests of a patented, brand-name drug manufacturer in enforcing its patent rights and the interests of the public in the availability of a competitively priced generic version of the drug as soon as possible. Given the infringement exemption under § 271(e)(1), § 271(e)(2) essentially authorizes a declaratory judgment suit by a patentee against a prospective infringer.

In *Merck KGaA v. Integra Lifesciences I, Ltd.*,[11] the Supreme Court held that 35 U.S.C. § 271(e)(1) extends to all uses of patented inventions that are reasonably related

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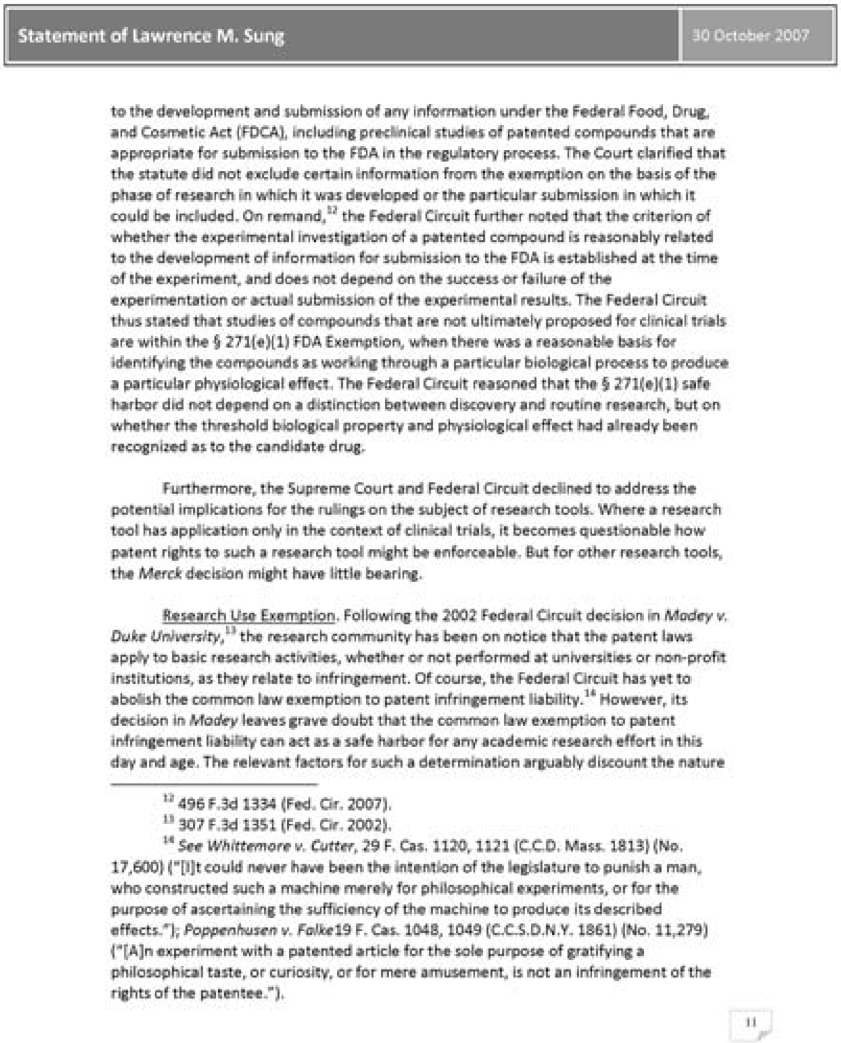
[10] *See, e.g.*, Board on Science, Technology, and Economic Policy, REAPING THE BENEFITS OF GENOMIC AND PROTEOMIC RESEARCH: INTELLECTUAL PROPERTY RIGHTS, INNOVATION AND PUBLIC HEALTH (Nat'l Academies Press 2006) ("Recommendation 11: NIH should undertake a study of potential university, government, and industry arrangements for the pooling and cross-licensing of genomic and proteomic patents, as well as research tools.").

[11] 545 U.S. 193 (2005).



to the development and submission of any information under the Federal Food, Drug, and Cosmetic Act (FDCA), including preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process. The Court clarified that the statute did not exclude certain information from the exemption on the basis of the phase of research in which it was developed or the particular submission in which it could be included. On remand,[12] the Federal Circuit further noted that the criterion of whether the experimental investigation of a patented compound is reasonably related to the development of information for submission to the FDA is established at the time of the experiment, and does not depend on the success or failure of the experimentation or actual submission of the experimental results. The Federal Circuit thus stated that studies of compounds that are not ultimately proposed for clinical trials are within the § 271(e)(1) FDA Exemption, when there was a reasonable basis for identifying the compounds as working through a particular biological process to produce a particular physiological effect. The Federal Circuit reasoned that the § 271(e)(1) safe harbor did not depend on a distinction between discovery and routine research, but on whether the threshold biological property and physiological effect had already been recognized as to the candidate drug.

Furthermore, the Supreme Court and Federal Circuit declined to address the potential implications for the rulings on the subject of research tools. Where a research tool has application only in the context of clinical trials, it becomes questionable how patent rights to such a research tool might be enforceable. But for other research tools, the *Merck* decision might have little bearing.

Research Use Exemption. Following the 2002 Federal Circuit decision in *Modey v. Duke University*,[13] the research community has been on notice that the patent laws apply to basic research activities, whether or not performed at universities or non-profit institutions, as they relate to infringement. Of course, the Federal Circuit has yet to abolish the common law exemption to patent infringement liability.[14] However, its decision in *Modey* leaves grave doubt that the common law exemption to patent infringement liability can act as a safe harbor for any academic research effort in this day and age. The relevant factors for such a determination arguably discount the nature of the defendant (whether academic, non-profit or not-for-profit in status) as well as the intent behind the conduct (non-pecuniary or non-commercial) as long as the act somehow can be related to a legitimate business purpose. Moreover, even where the experimental work can be shown to occur outside the umbrella of a research institution or other enterprise, the protection of the common law exemption to patent infringement liability likely will not extend to activity other than hobbyist tinkering or testing of a patented invention for verification and reproducibility.

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[12] 496 F.3d 1334 (Fed. Cir. 2007).

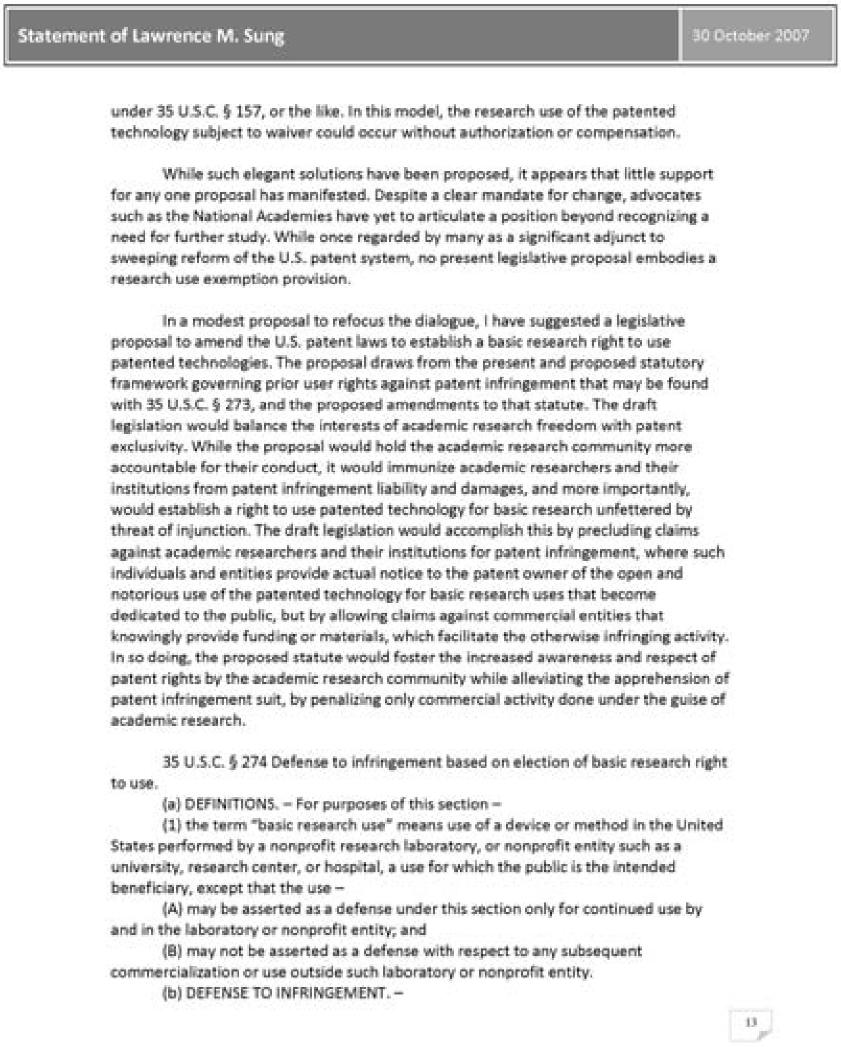
[13] 307 F.3d 1351 (Fed. Cir. 2002).

[14] *See Whittemore v. Cutter*, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) (No. 17,600) ("[I]t could never have been the intention of the legislature to punish a man, who constructed such a machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects."); *Poppenhusen v. Falke*19 F. Cas. 1048, 1049 (C.C.S.D.N.Y. 1861) (No. 11,279) ("[A]n experiment with a patented article for the sole purpose of gratifying a philosophical taste, or curiosity, or for mere amusement, is not an infringement of the rights of the patentee.").

The theoretical constructs behind § 271(e)(1) and other legislation, extant or proposed, to exempt certain activities from patent infringement liability all flow from specific policy considerations beyond the diverse objectives that are offset in a delicate interplay to promote the progress of the useful arts. The divergence, therefore, that rests with a proposal to establish a universal statutory research use exemption, without regard to technology, industry or regulatory concerns, is the need to reassess the very nature of the patent system.

The literature is rich with excellent considerations of this topic. Indeed, commentators, like Professors Janice Mueller, Katherine Strandburg, and Rochelle Dreyfuss, have set forth sound rationales for a research use exemption, whereas others like Professor Richard Epstein have advocated that compulsory licensing, experimental use defenses, condemnation proceedings, and such, which assertedly reflect *ad hoc* interventions, defy the reality that the extant system works acceptably.

Prior, more broad-based, approaches included aspects of compulsory licensing. In this vein, for example, Professor Mueller's proposed a standard reach-through royalty of 25% of pre-tax profits. Professor Strandburg further proposed a two-tiered compulsory licensing scheme for research tool patents. In this regard, research tool patents would be entitled to three to five years of default exclusivity, after which compulsory licensing could apply. This approach, according to Professor Strandburg, would encourage early commercialization and voluntary licensing. Such an outcome seems likely, particularly if voluntary licensing during the exclusivity period prescribes some benchmark for the royalty rate applied during the compulsory licensing period. Professor Dreyfuss raised detailed insights into a balancing of the benefits and harms between patentee and basic researchers in her proposal for special liability rules attached to research uses of patented technology. One suggestion was a statutory amendment to exempt basic research from patent infringement remedies, similar to 35 U.S.C. § 287(c)(2) for certain uses of patented surgical and medical methods. Professor Dreyfuss alternatively (and more favorably) advocated a waiver registry that enabled basic researchers to gain access to a patented technology by executing a written waiver that publicly dedicated any subject matter discovered or invented through the use of the patented technology. The dedication to the public under the Dreyfuss proposal would take the form of novelty-defeating publication, statutory invention registration



under 35 U.S.C. § 157, or the like. In this model, the research use of the patented technology subject to waiver could occur without authorization or compensation.

While such elegant solutions have been proposed, it appears that little support for any one proposal has manifested. Despite a clear mandate for change, advocates such as the National Academies have yet to articulate a position beyond recognizing a need for further study. While once regarded by many as a significant adjunct to sweeping reform of the U.S. patent system, no present legislative proposal embodies a research use exemption provision.

In a modest proposal to refocus the dialogue, I have suggested a legislative proposal to amend the U.S. patent laws to establish a basic research right to use patented technologies. The proposal draws from the present and proposed statutory framework governing prior user rights against patent infringement that may be found with 35 U.S.C. § 273, and the proposed amendments to that statute. The draft legislation would balance the interests of academic research freedom with patent exclusivity. While the proposal would hold the academic research community more accountable for their conduct, it would immunize academic researchers and their institutions from patent infringement liability and damages, and more importantly, would establish a right to use patented technology for basic research unfettered by threat of injunction. The draft legislation would accomplish this by precluding claims against academic researchers and their institutions for patent infringement, where such individuals and entities provide actual notice to the patent owner of the open and notorious use of the patented technology for basic research uses that become dedicated to the public, but by allowing claims against commercial entities that knowingly provide funding or materials, which facilitate the otherwise infringing activity. In so doing, the proposed statute would foster the increased awareness and respect of patent rights by the academic research community while alleviating the apprehension of patent infringement suit, by penalizing only commercial activity done under the guise of academic research.

35 U.S.C. § 274 Defense to infringement based on election of basic research right to use.

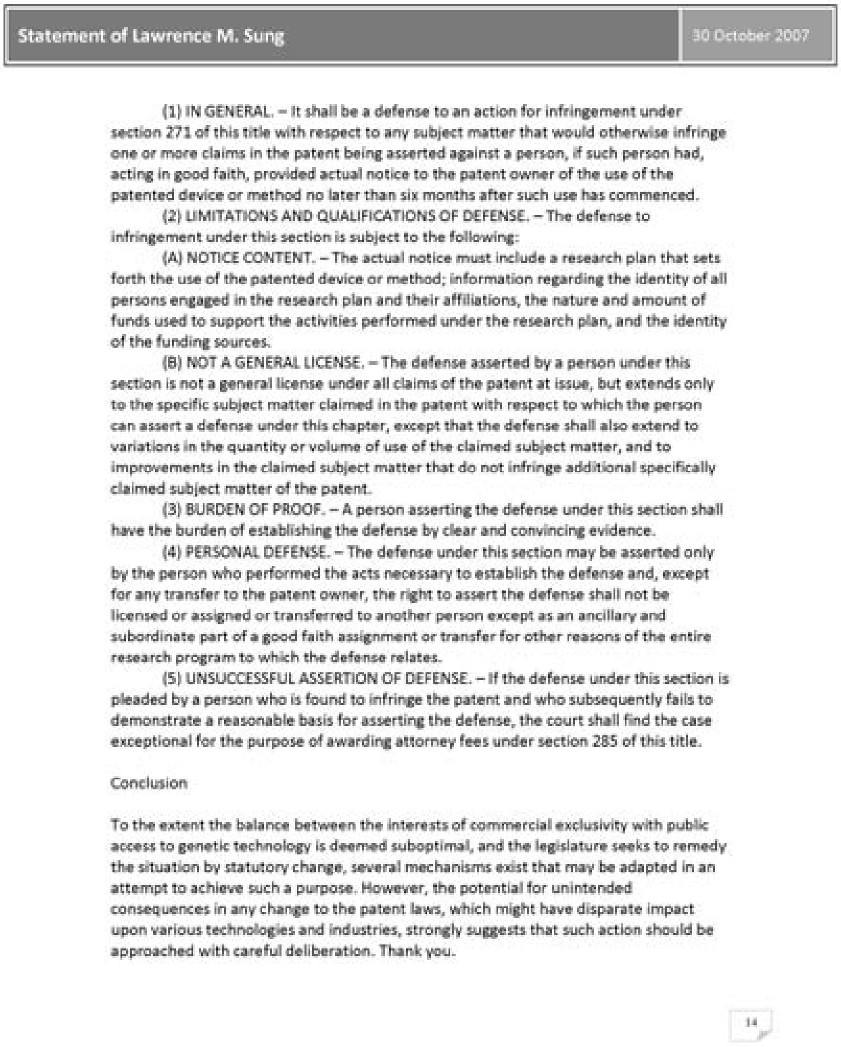
(a) DEFINITIONS. – For purposes of this section –

(1) the term "basic research use" means use of a device or method in the United States performed by a nonprofit research laboratory, or nonprofit entity such as a university, research center, or hospital, a use for which the public is the intended beneficiary, except that the use –

(A) may be asserted as a defense under this section only for continued use by and in the laboratory or nonprofit entity; and

(B) may not be asserted as a defense with respect to any subsequent commercialization or use outside such laboratory or nonprofit entity.

(b) DEFENSE TO INFRINGEMENT. –



(1) IN GENERAL. – It shall be a defense to an action for infringement under section 271 of this title with respect to any subject matter that would otherwise infringe one or more claims in the patent being asserted against a person, if such person had, acting in good faith, provided actual notice to the patent owner of the use of the patented device or method no later than six months after such use has commenced.

(2) LIMITATIONS AND QUALIFICATIONS OF DEFENSE. – The defense to infringement under this section is subject to the following:

(A) NOTICE CONTENT. – The actual notice must include a research plan that sets forth the use of the patented device or method; information regarding the identity of all persons engaged in the research plan and their affiliations, the nature and amount of funds used to support the activities performed under the research plan, and the identity of the funding sources.

(B) NOT A GENERAL LICENSE. – The defense asserted by a person under this section is not a general license under all claims of the patent at issue, but extends only to the specific subject matter claimed in the patent with respect to which the person can assert a defense under this chapter, except that the defense shall also extend to variations in the quantity or volume of use of the claimed subject matter, and to improvements in the claimed subject matter that do not infringe additional specifically claimed subject matter of the patent.

(3) BURDEN OF PROOF. – A person asserting the defense under this section shall have the burden of establishing the defense by clear and convincing evidence.

(4) PERSONAL DEFENSE. – The defense under this section may be asserted only by the person who performed the acts necessary to establish the defense and, except for any transfer to the patent owner, the right to assert the defense shall not be licensed or assigned or transferred to another person except as an ancillary and subordinate part of a good faith assignment or transfer for other reasons of the entire research program to which the defense relates.

(5) UNSUCCESSFUL ASSERTION OF DEFENSE. – If the defense under this section is pleaded by a person who is found to infringe the patent and who subsequently fails to demonstrate a reasonable basis for asserting the defense, the court shall find the case exceptional for the purpose of awarding attorney fees under section 285 of this title.

Conclusion

To the extent the balance between the interests of commercial exclusivity with public access to genetic technology is deemed suboptimal, and the legislature seeks to remedy the situation by statutory change, several mechanisms exist that may be adapted in an attempt to achieve such a purpose. However, the potential for unintended consequences in any change to the patent laws, which might have disparate impact upon various technologies and industries, strongly suggests that such action should be approached with careful deliberation. Thank you.

Mr. BERMAN. Thank you very much, Dr. Sung.

Mr. Soderstrom?

TESTIMONY OF E. JONATHAN SODERSTROM, MANAGING DIRECTOR, OFFICE OF COOPERATIVE RESEARCH, YALE UNIVERSITY, NEW HAVEN, CT

Mr. SODERSTROM. Thank you, Mr. Chairman, for the invitation to be here today.

As you indicated in your opening statement, some scholars have argued that patents and their enforcement may impose significant costs upon noncommercial biomedical research by creating an anti-commons or a patent thicket that may make the acquisition of licenses and other rights too burdensome to permit the pursuit of these otherwise scientifically and socially worthwhile research. These concerns have grown since the *Madey v. Duke* decision that affirmed the affirmation of any research exemption shielding universities from patent infringement liability.

Without diminishing the importance of these potential concerns, it should be pointed out that the evidence offered to support these contentions is primarily anecdotal, and I need not remind you that the plural of anecdote is not data. Although a few isolated incidents have received significant attention, there is little systematic evidence that widespread assertion of patent rights on genes has been significantly hampered biomedical research.

Two recent surveys, as you pointed out, offer little empirical basis for claims that restricted access to intellectual property is currently impeding academic biomedical research. The authors, in fact, further note that patents are not typically used to restrict access to knowledge and tangible materials that biomedical scientists require.

The surveys further show that firms generally do not threaten infringement litigation against academic research institutions, a de factor research exemption, if you will, in part because such academic use may improve their invention or because they wish to maintain good will and ensure access to future academic inventions and also because the damages, as we all know, are likely to be very small.

These studies also confirm that university technology managers take a very nuanced approach to patenting and licensing seeking only enough intellectual property protection to facilitate the commercial development of an invention. Decisions to patent and strategies for commercializing the inventions depend on a determination of the level of protection necessary to induce an interested company into investing in the further development, testing, manufacturing, marketing, sales of a product embodying the technology.

But these results should not be surprising. The practice of university technology transfer managers reflect the salutary effects of the guidance that the National Institutes of Health has issued on patenting of research tools and genomic inventions as well as the formation of professional norms and standards of behavior encouraged by groups, such as the one that I help lead, the Association of University Technology Managers.

Universities share certain core values, and we seek to maintain to the fullest extent possible in all technology transfer agreements.

Chief among these values are the protection of academic freedom and the open pursuit of scientific inquiry. We seek balance between the business needs of our licensing partners and the shared value of our respective academic institutions.

Recently, a group of university research officers, licensing directors, and a representative from the Association of American Medical Colleges recognized the need to clearly articulate a set of principles that strike such an appropriate public policy balance.

The participating universities released a white paper in the public interest, nine points to consider in licensing university technology. These considerations were put forth in an aspirational or self-correcting sense to encourage the profession to set a high standard by creatively stretching the boundaries of conventional and licensing practices and ensuring that licensing activities are in the public interest for society's benefits.

The nine points included: one, universities should reserve the right to practice licensed inventions and to allow other nonprofit and governmental organizations to do so; two, exclusive licenses should be structured in a manner that encourage technology development and use as broadly and as quickly as possible; three, that we should strive to minimize the licensing of "future improvements"; four, that universities should anticipate and help manage technology transfer-related conflicts of interest; five, ensure broad access to research tools; six, enforcement action should be carefully considered; seven, we should be mindful of export regulations; eight, we should be mindful of the implications of working with patent aggregators; and, nine, we should consider including provisions that address unmet needs, such as those of neglected patient populations or geographic areas, giving particular attention to improved therapeutics, diagnostics and agricultural technologies for the developing world.

Many of these points were already being practiced. In fact, the nine points have been endorsed by a growing number of academic institutions and professional organizations around the world. We applaud these participating universities' efforts to articulate these important principles and urge their adoption and application by the wider community of universities.

In the end, we hope to foster thoughtful approaches and creative solutions to complex problems that may arise when universities license technologies in the public interest and for society's benefit. We believe that patent policy, as well as practice, should be guided by the goal of promoting innovation and, in turn, improvements in human welfare.

That view drove Yale's interest in helping to draft the nine points guidelines, which recommended that universities endeavor to make genomic inventions that will serve primarily as research tools as broadly available as possible.

Yale has long taken a balanced approach to patenting, taking into account the nature of the invention, its relevance to research, and the extent to which patent protection would be necessary to give a commercial partner adequate incentive to develop the product completely. We have taken a similar approach to licensing, especially by insisting on the right to make the invention available to researchers at Yale and other academic institutions.

We do not think that gene patents are having a significant negative impact on academic research. There have been thoughtful analyses of problems that could arise, but the most comprehensive studies of this issue concluded that the patents are not slowing the pace of research.

Yale and other research universities have a major stake in ensuring access to research tools. We also recognize that circumstances may change as the field of genomics and proteomics continue to advance, and I am confident that the scientific community, working with the National Institutes of Health, the Association of Technology Managers, the Association of American Medical Colleges and others, will continue to monitor whether gene patents are interfering significantly with research.

My colleagues and I are grateful for the Subcommittee's interest in this topic.

Thank you.

[The prepared statement of Mr. Soderstrom follows:]

PREPARED STATEMENT OF E. JONATHAN SODERSTROM

Mr. Chairman, thank you for the opportunity to testify before your Subcommittee on the topic of whether gene patents are helping or hurting research in the life sciences.

My name is Jon Soderstrom. I am the Managing Director of the Office of Cooperative Research (OCR) at Yale University. The Office of Cooperative Research is the intellectual property management and licensing organization for Yale University. I also serve as the President-Elect for the Association of University Technology Managers known as AUTM. AUTM is a nonprofit organization created to function as a professional and educational society for academic technology transfer professionals involved with the management of intellectual property. AUTM was founded in 1974 as the Society of University Patent Administrators. That group laid the foundation for the association that exists today with more than 3,000 members strong representing over 1,500 institutions and companies across the globe.

SOURCES OF CONCERN

Scholars have recently argued that patents may impose significant costs upon noncommercial biomedical research. Heller and Eisenberg[1] suggest that the patenting of a broad range of the inputs that researchers need to do their work may give rise to an "anti-commons" or "patent thicket" that may make the acquisition of licenses and other rights too burdensome to permit the pursuit of what should otherwise be scientifically and socially worthwhile research. Merges and Nelson[2] and Scotchmer[3] highlight the related possibility that, in some fields of technology, the assertion of patents on only one or two key upstream, foundational discoveries may significantly restrict follow-on research. A further concern is that the prospect of realizing financial gain from upstream research may make researchers reluctant to share information or research materials with one another, thereby impeding the realization of research efficiencies and complementarities. Similarly, researchers may be trading away rights to conduct future research or to freely disseminate their discoveries in exchange for current access to research inputs or financial support.[4] Finally, prospective financial gains from the exploitation of intellectual property may induce researchers to choose research projects on the basis of commercial potential rather than scientific merit.

Another aspect of the debate about whether intellectual property fosters or hinders biomedical research relates to the 'research tools,' which are the ideas, data, materials or methods used to conduct research. Many such materials and methods are disclosed or claimed in DNA patents. Among DNA patents, there is particular concern about the subset of gene patents and their relevance to research tools because genes are not only inputs to developing genetic tests and therapeutic proteins, and thus directly relevant to medically important products and services, but also are crucially important tools for ongoing research. Concern over the impact of patenting and licensing on biomedical research has grown since the Court of Appeals for the Federal Circuit's 2002 *Madey v. Duke* decision, which visibly affirmed the absence of any research exemption shielding universities from patent infringement liability. Patent claims based on DNA sequences can be infringed by research activities that entail making or using the claimed sequence, not just by selling products or services.

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[1] Heller, M.A. and Eisenberg, R. S. 1998. "Can Patents Deter Innovation? The Anti-Commons in Biomedical Research." *Science,* Vol. 280. No. 5364, pp. 698–701

[2] Merges, R. P. and R. R. Nelson. 1990. "On the Complex Economics of Patent Scope. "Columbia Law Review 90:839–916

[3] Scotchmer, S. 1991. "Standing on the Shoulders of Giants: Cumulative Research and the Patent Law." *Journal of Economic Perspectives* 5:29–41.

[4] Cohen, W. M., R. Florida, and R. Goe. 1994. "University-Industry Research Centers in the United States."; Thursby, Jerry G. and Marie C. Thursby. 2003. "University Licensing and the Bayh-Dole Act." *Science* 301:1052.

Without diminishing the importance of these potential concerns, it should be pointed out that the evidence offered to support these contentions is primarily anecdotal. Although these isolated instances have received significant attention, there is no evidence that widespread assertion of patent rights on genes has significantly hampered biomedical research. Contrary to these prevailing beliefs, findings from a recent survey of 414 biomedical researchers in universities, government, and nonprofit institutions offers little empirical basis for claims that restricted access to intellectual property is currently impeding academic biomedical research.[5] The authors noted that, although common, patents in this field are not typically used to restrict access to the knowledge and tangible materials that biomedical scientists require.

The authors cite a number of reasons, including the fact that firms generally do not threaten infringement litigation against academic research institutions (a *de facto* research exemption), in part because such academic use may improve their invention, because they wish to maintain good will and to ensure access to future academic inventions, and also because the damages are likely to be very small. According to the authors:

> "Our research thus suggests that 'law on the books' need not be the same as 'law in action' if the law on the books contravenes a community's norms and interests."

These findings are consistent with another recent major survey of 19 of the 30 US universities with the largest number of DNA patents. Their results showed that the licensing of DNA patents at US academic institutions has not led to the decline in academic cooperation and technology transfer that many observers have feared.[6] In fact, based on responses, the study demonstrated that in most cases the licensing behavior of universities allows for collaboration and sharing of DNA-based inventions among academic institutions.

The study investigated the patenting and licensing behavior for four main types of DNA-based inventions:

- DNA sequences that encode therapeutic proteins
- DNA sequences that are phenotypic markers only
- DNA sequences comprising genes encoding drug targets
- DNA discoveries or inventions representing research tools

The authors discovered that most universities base their decisions to patent and strategies for commercializing the invention on a determination of the level of protection necessary to induce an interested company into investing in the further development, testing, manufacture, marketing and sales of a product embodying the technology. Thus, in the case of a fully sequenced gene that encodes a therapeutic protein, where the utility and the development risks are both generally acknowledged to be high, survey respondents generally agreed that they would patent and license such inventions exclusively. However, in the case where the gene encoded is simply a target for drug discovery, few would consider even patenting such a discovery since researchers would be free to screen their compound libraries against the target while the patent application was pending and to use any resulting information without fear on infringement. In addition, it has become commonplace for universities, when licensing their inventions, to reserve the right for their own faculty, as well as researchers at other non-profit entities, to use the patented invention. The study confirmed that university technology managers take a nuanced approach to patenting and licensing, seeking only enough intellectual property protection to facilitate the commercial development of the invention.

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[5] Walsh, J. P. Cho, C. Cohen, W. M. 2005. "View from the Bench: Patents and Material Transfers." *Science* 309: 2002–2003.

[6] Pressman, L. Burgess, R. Cook-Deegan, R. M. McCormack, S. J. Nami-Wolk, I. Soucy, M. & Walters, L. 2006. "The Licensing of DNA Patents by US Academic Institutions: An Empirical Survey." *Nature Biotechnology* 24: 31–39.

This market sensitivity is also reflected in data on patent trends. The number of DNA patents has shown a fairly dramatic and steady decline since their peak in 2001 (from about 4,500 to around 2,700 in 2005). Patent prosecution, maintenance and management costs that are typically between $20,000 and $30,000 per patent militate against patenting inventions that are unlikely to recover those costs and encourage considerable selectivity in which inventions are patented. As Pressman et al. point out, "these practices are designed pragmatically to accommodate both economic goals, such as revenue generation and new company formation, and social goals, such as ensuring utilization and availability of federally funded inventions."

ESTABLISHING LICENSING PRINCIPLES TO PROMOTE ACCESS

These results are not surprising to persons currently involved in technology licensing activities as practiced at major research universities. To some extent the practices of university technology transfer managers reflect the salutary effects of guidance that the National Institutes of Health has issued on patenting of research tools and genomic inventions as well as the formation of professional norms and standards of behavior encouraged by groups such as the Association of University Technology Managers. Universities share certain core values that can and should be maintained to the fullest extent possible in all technology transfer agreements, chief among these are the protection of academic freedom and open pursuit of scientific inquiry. When crafting agreements with industry, a balance must be struck between the business needs of our licensing partners to generate returns on their investments and the shared values of our respective academic institutions.

Recognizing the need to clearly articulate a set of technology licensing principles that strikes the appropriate balance, a group of university research officers, licensing directors and a representative from the Association of American Medical Colleges met in July 2006 to brainstorm about critical societal, policy, legislative and other issues in university technology transfer.[7] Our aim was and is to encourage our colleagues in the academic technology transfer profession to analyze each licensing opportunity individually, but with certain core principles in mind.

The participating universities released a white paper, "In the Public Interest: Nine Points to Consider in Licensing University Technology."[8] The paper seeks to capture the shared perspectives of the participating university research officers and licensing directors on policy issues related to university technology transfer, in particular, with respect to ensuring that licensing activities are "in the public interest and for society's benefit." These considerations are put forth in an aspirational, rather than proscriptive, sense to encourage others in the profession to set a higher standard by stretching the boundaries of conventional licensing practices and sharing with the greater technology transfer community the insights that they gain in doing so.

The nine points identified in the white paper (see Appendix for the full elaboration of each point) included:

Point 1: Universities should reserve the right to practice licensed inventions and to allow other non-profit and governmental organizations to do so

Point 2: Exclusive licenses should be structured in a manner that encourages technology development and use

Point 3: Strive to minimize the licensing of "future improvements"

Point 4: Universities should anticipate and help to manage technology transfer related conflicts of interest

Point 5: Ensure broad access to research tools

Point 6: Enforcement action should be carefully considered

Point 7: Be mindful of export regulations

Point 8: Be mindful of the implications of working with patent aggregators

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[7] The participating universities included: California Institute of Technology, Cornell University, Harvard University, Massachusetts Institute of Technology, Stanford University, University of California, University of Illinois, Chicago, University of Illinois, Urbana-Champaign, University of Washington, Wisconsin Alumni Research Foundation, Yale University and Association of American Medical Colleges (AAMC).

[8] "In the Public Interest: Nine Points to Consider in University Licensing," March 6, 2007. *http://www.autm.org/aboutTT/Points*__to__Consider.pdf

Point 9: Consider including provisions that address unmet needs, such as those of neglected patient populations or geographic areas, giving particular attention to improved therapeutics, diagnostics and agricultural technologies for the developing world

IN CONCLUSION

As technology transfer professionals, we recognize that many of these points are already being practiced. In fact, these points have been endorsed by a growing number of institutions and professional organizations around the world. We applaud the participating institutions' efforts to articulate these important principles and urge their adoption and application by the wider community of universities. As often is the case, guidance as to implementation of practices that will advance the mission of university technology transfer lags behind our collective awareness of both the needs that exist and our role in fostering an environment in which such needs can be met effectively. Given recent criticism from some sectors that question the motives and methods underlying university technology commercialization activities, however, it is especially important that the principles used to support our decision-making be recognized as serving the best interest of the public not just of individual universities. Beyond the simple economics of any agreement, it is our hope that our colleagues will give serious consideration to these additional points before finalizing the terms and conditions of any technology transfer agreement. In the end, we hope to foster thoughtful approaches and encourage creative solutions to complex problems that may arise when universities license technologies in the public interest and for society's benefit.

We believe that patent policy, as well as practice, should be guided by the goal of promoting innovation and, in turn, improvements in human welfare. That view drove Yale's interest in helping to draft the "Nine Points" guidelines, which recommend that universities refrain from patenting genomic inventions that will serve primarily as research tools. Yale has long taken a balanced approach to patenting, taking into account the nature of the invention, its relevance to research, and the extent to which patent protection would be necessary to give a commercial partner adequate incentive to develop the product completely. We have taken a similar approach to licensing, especially by insisting upon the right to make the invention available to researchers at Yale and other academic institutions.

We do not think that gene patents are having a significant negative impact on academic research. There have been thoughtful analyses of problems that could arise, and there have been anecdotal reports and two comprehensive studies of this issue, cited earlier in my testimony, that concluded that patents are not slowing the pace of research for several reasons. Universities take a nuanced approach to patenting and they are increasingly making specific provision for research uses of inventions in licenses. There is evidence that a "de facto research exemption" exists because companies rarely prosecute academic investigators for research uses that may be infringing.

Yale and other universities have a major stake in ensuring that access to research tools is not compromised (the "Nine Points" document is evidence of that); we also recognize that circumstances may change as the fields of genomics and proteomics continue to advance. I am confident that the scientific community, working with the National Institutes of Health, the Association of University Technology Managers, the Association of American Medical Colleges and others, we will continue to monitor whether gene patents are interfering significantly with research. My colleagues and I are grateful for the Subcommittee's interest in this topic.

APPENDIX

In the Public Interest:
Nine Points to Consider in Licensing University Technology

Point 1

Universities should reserve the right to practice licensed inventions and to allow other non-profit and governmental organizations to do so

In the spirit of preserving the ability of all universities to perform research, ensuring that researchers are able to publish the results of their research in dissertations and peer-reviewed journals and that other scholars are able to verify published results without concern for patents, universities should consider reserving rights in all fields of use, even if the invention is licensed exclusively to a commercial entity, for themselves and other non-profit and governmental organizations:

- to practice inventions and to use associated information and data for research and educational purposes, including research sponsored by commercial entities; and
- to transfer tangible research materials (e.g., biological materials and chemical compounds) and intangible materials (e.g., computer software, databases and know-how) to others in the non-profit and governmental sectors.

Clear articulation of the scope of reserved rights is critical.

Point 2

Exclusive licenses should be structured in a manner that encourages technology development and use

When significant investment of time and resources in a technology are needed in order to achieve its broad implementation, an exclusive license often is necessary and appropriate. However, it is important that technology transfer offices be aware of the potential impact that the exclusive license might have on further research, unanticipated uses, future commercialization efforts and markets. Universities need to be mindful of the impact of granting overly broad exclusive rights and should strive to grant just those rights necessary to encourage development of the technology.

Special consideration should be given to the impact of an exclusive license on uses of a technology that may not be appreciated at the time of initial licensing. A license grant that encompasses all fields of use for the life of the licensed patent(s) may have negative consequences if the subject technology is found to have unanticipated utility. This possibility is particularly troublesome if the licensee is not able or willing to develop the technology in fields outside of its core business. Universities are encouraged to use approaches that balance a licensee's legitimate commercial needs against the university's goal (based on its educational and charitable mission and the public interest) of ensuring broad practical application of the fruits of its research programs.

In situations where an exclusive license is warranted, it is important that licensees commit to diligently develop the technology to protect against a licensee that is unable or unwilling to move an innovation forward. In long-term exclusive licenses, diligent development should be well-defined and regularly monitored during the exclusive term of the agreement and should promote the development and broad dissemination of the licensed technology. Ideally, objective, time-limited performance milestones are set, with termination or non-exclusivity (subject to limited, but reasonable, cure provisions) as the penalty for breach of the diligence obligation.

Another means of ensuring diligent development, often used in conjunction with milestones, is to require exclusive licensees to grant sublicenses to third parties to address unmet market or public health needs ("mandatory sublicensing") and/or to diligently commercialize new applications of the licensed rights. Such a requirement could also be implemented through a reserved right of the licensor to grant direct licenses within the scope of the exclusive grant to third parties based on unmet need. In such situations, it is important to ensure that the parties have a common understanding of what constitutes a new application or unmet need for the purpose of implementing such a provision.

Absent the need for a significant investment—such as to optimize a technology for wide use—broad, non-exclusive licensing of tools such as genomic and proteomic inventions can help maximize the benefits derived from those technologies, in part by removing obstacles to further innovation. Unlike most research tools or manufacturing methods, diagnostic tests often must go through the regulatory approval process, and so may warrant exclusive licensing when the costs of test development, approval or diffusion require substantial investment of capital. Nevertheless, licensing of diagnostic tests based on broadly applicable genomics or proteomics methods should strive to preserve sufficient flexibility to permit testing for multiple indications (i.e., not an exclusive licensee's single disease of interest) perhaps through multiple field-restricted or non-exclusive licenses. Exclusive licensing of a single gene for a diagnostic may be counterproductive in a multi-gene pathology where only a panel of genes can yield an adequate diagnosis, unless the licensee has access to the other genes of the panel. Such licenses can also be limited in other ways. For example, a university might license a genomics method exclusively for a company to optimize and sell licensed products for diagnostic use. The drafting of the exclusive grant could make it clear that the license is exclusive for the sale, *but not use,* of such products; in doing so, the university ensures that it is free to license non-exclusively to others the right (or may simply not assert its rights) to use the patented technology, which they may do either using products purchased from the exclusive licensee or those that they make in-house for their own use.

In general, when no alternative testing strategy is available for a given indication, consideration should be given to means of ensuring reasonable access for patients and shielding individual healthcare providers from the risk of suit for patent infringement. As with any medical technology, licenses should not hinder clinical research, professional education and training, use by public health authorities, independent validation of test results or quality verification and/or control.

Point 3

Strive to minimize the licensing of "future improvements"

Although licensees often seek guaranteed access to future improvements on licensed inventions, the obligation of such future inventions may effectively enslave a faculty member's research program to the company, thereby exerting a chilling effect on their ability to receive corporate and other research funding and to engage in productive collaborations with scientists employed by companies other than the licensee—perhaps even to collaborate with other academic scientists. In particular, if such future rights reach to inventions made elsewhere in the university, researchers who did not benefit from the licensing of the original invention may have their opportunities restricted as well, and may be disadvantaged economically relative to the original inventors if the licensing office has pre-committed their inventions to a licensee.

For these reasons, exclusive licensees should not automatically receive rights to "improvement" or "follow-on" inventions. Instead, as a matter of course, licensed rights should be limited to existing patent applications and patents, and only to those claims in any continuing patent applications that are (i) fully supported by information in an identified, existing patent application or patent and (ii) entitled to the priority date of that application or patent.

In the rare case where a licensee is granted rights to improvement patents, it is critical to limit the scope of the grant so that it does not impact uninvolved researchers and does not extend indefinitely into the future. It is important to further restrict the grant of improvements to inventions that are owned and controlled by the licensor institution—i.e., (i) not made by the inventor at another institution, should they move on or (ii) co-owned with, or controlled by, another party. One refinement to this strategy would be to limit the license to inventions that are dominated by the original licensed patents, as these could not be meaningfully licensed to a third party, at least within the first licensee's exclusive field. As was discussed earlier, appropriate field restrictions enable the licensing not only of the background technology, but also of improvements, to third parties for use outside the initial licensee's core business. In all cases, a license to improvements should be subject to appropriate diligent development requirements.

It should be recognized, however, that not all "improvements" have commercial potential (for example, they may not confer sufficient additional benefit over the existing technology to merit the expense of the development of new or modified products), in which case a licensee might not wish to develop them. In general, it may be best simply not to patent such improvements.

Point 4

Universities should anticipate and help to manage technology transfer related conflicts of interest

Technology transfer offices should be particularly conscious and sensitive about their roles in the identification, review and management of conflicts of interest, both at the investigator and institutional levels. Licensing to a start-up founded by faculty, student or other university inventors raises the potential for conflicts of interest; these conflicts should be properly reviewed and managed by academic and administrative officers and committees outside of the technology transfer office. A technology licensing professional ideally works in an open and collegial manner with those directly responsible for oversight of conflicts of interest so as to ensure that potential conflicts arising from licensing arrangements are reviewed and managed in a way that reflects well on their university and its community. Ideally, the university has an administrative channel and reporting point whereby potential conflicts can be non-punitively reported and discussed, and through which consistent decisions are made in a timely manner.

Point 5

Ensure broad access to research tools

Consistent with the NIH Guidelines on Research Tools, principles set forth by various charitable foundations that sponsor academic research programs and by the mission of the typical university to advance scientific research, universities are expected to make research tools as broadly available as possible. Such an approach is in keeping with the policies of numerous peer-reviewed scientific journals, on which the scientific enterprise depends as much as it does on the receipt of funding: in order to publish research results, scientists must agree to make unique resources (e.g., novel antibodies, cell lines, animal models, chemical compounds) available to others for verification of their published data and conclusions.

Through a blend of field-exclusive and non-exclusive licenses, research tools may be licensed appropriately, depending on the resources needed to develop each particular invention, the licensee's needs and the public good. As suggested with respect to genomics and proteomics method patents in Point 2 above, a university might license a research reagent, kit or device exclusively to a company to optimize and sell licensed products and services for research, diagnostic or other end uses. The drafting of such an exclusive grant should make clear that the license is exclusive for the sale, *but not use,* of such products and services; in doing so, the university ensures that it is free to license non-exclusively to others the right to use the patented technology, which they may do either using products purchased from the exclusive licensee or those that they make in-house for their own use.

Point 6

Enforcement action should be carefully considered

In considering enforcement of their intellectual property, it is important that universities be mindful of their primary mission to use patents to promote technology development for the benefit of society. All efforts should be made to reach a resolution that benefits both sides and promotes the continuing expansion and adoption of new technologies. Litigation is seldom the preferred option for resolving disputes.

However, after serious consideration, if a university still decides to initiate an infringement lawsuit, it should be with a clear, mission-oriented rationale for doing so—one that can be clearly articulated both to its internal constituencies and to the public. Ideally, the university's decision to litigate is based on factors that closely track the reasons for which universities obtain and license patents in the first place, as set out elsewhere in this paper. Examples might include:

- Contractual or ethical obligation to protect the rights of existing licensees to enjoy the benefits conferred by their licenses; and
- Blatant disregard on the part of the infringer for the university's legitimate rights in availing itself of patent protection, as evidenced by refusal on the part of the infringer to negotiate with or otherwise entertain a reasonable offer of license terms.

Under all circumstances, it reflects poorly on universities to be involved in "nuisance suits." Exclusive licensees should be encouraged to approach patent enforcement in a manner that is consistent with the philosophy described in this Point 6.

Point 7

Be mindful of export regulations

University technology transfer offices should have a heightened sensitivity about export laws and regulations and how these bodies of law could affect university licensing practices. Licensing "proprietary information" or "confidential information" can affect the "fundamental research exclusion" (enunciated by the various export regulations) enjoyed by most university research, so the use of appropriate language is particularly important. Diligence in ensuring that technology license transactions comply with federal export control laws helps to safeguard the continued ability of technology transfer offices to serve the public interest.

Point 8

Be mindful of the implications of working with patent aggregators

As is true of patents generally, the majority of university-owned patents are unlicensed. With increasing frequency, university technology transfer offices are approached by parties who wish to acquire rights in such 'overstock' in order to commercialize it through further licenses. These patent aggregators typically work under one of two models: the 'added value' model and the so-called 'patent troll' model.

Under the added value model, the primary licensee assembles a portfolio of patents related to a particular technology. In doing so, they are able to offer secondary licensees a complete package that affords them freedom to operate under patents perhaps obtained from multiple sources. As universities do not normally have the resources to identify and in-license relevant patents of importance, they cannot offer others all of the rights that may control practice (and, consequently, commercialization) of university inventions. By consolidating rights in patents that cover foundational technologies and later improvements, patent aggregators serve an important translational function in the successful development of new technologies and so exert a positive force toward commercialization. For example, aggregation of patents by venture capital groups regularly results in the establishment of corporate entities that focus on the development of new technologies, including those that arise from university research programs. To ensure that the potential benefits of patent aggregation actually are realized, however, license agreements, both primary and secondary, should contain terms (for example, time-limited diligence requirements) that are consistent with the university's overarching goal of delivering useful products to the public.

In contrast to patent aggregators who add value through technology-appropriate bundling of intellectual property rights, there are also aggregators (the 'patent trolls') who acquire rights that cut broadly across one or more technological fields with no real intention of commercializing the technologies. In the extreme case, this kind of aggregator approaches companies with a large bundle of patent rights with the expectation that they license the entire package on the theory that any company that operates in the relevant field(s) must be infringing at least one of the hundreds, or even thousands, of included patents. Daunted by the prospect of committing the human and financial resources needed to perform due diligence sufficient to establish their freedom to operate under each of the bundled patents, many companies in this situation will conclude that they must pay for a license that they may not need. Unlike the original patent owner, who has created the technology and so is reasonably entitled to some economic benefit in recognition for its innovative contribution, the commercial licensee who advances the technology prior to sublicensing, or the added value aggregator who helps overcome legal barriers to product development, the kind of aggregator described in this paragraph typically extracts payments in the absence of any enhancement to the licensed technology.[9] Without delving more deeply into the very real issues of patent misuse and bad-faith dealing by such aggregators, suffice it to say that universities would better serve the public interest by ensuring appropriate use of their technology by requiring their licensees to operate under a business model that encourages commercialization and does not rely primarily on threats of infringement litigation to generate revenue.

Point 9

Consider including provisions that address unmet needs, such as those of neglected patient populations or geographic areas, giving particular attention to improved therapeutics, diagnostics and agricultural technologies for the developing world

Universities have a social compact with society. As educational and research institutions, it is our responsibility to generate and transmit knowledge, both to our students and the wider society. We have a specific and central role in helping to advance knowledge in many fields and to manage the deployment of resulting innovations for the public benefit. In no field is the importance of doing so clearer than it is in medicine.

Around the world millions of people are suffering and dying from preventable or curable diseases. The failure to prevent or treat disease has many causes. We have a responsibility to try to alleviate it, including finding a way to share the fruits of what we learn globally, at sustainable and affordable prices, for the benefit of the world's poor. There is an increased awareness that responsible licensing includes consideration of the needs of people in developing countries and members of other underserved populations.

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[9] A somewhat related issue is that of technology 'flipping', wherein a non-aggregator licensee of a university patent engages in sublicensing without having first advanced the technology, thereby increasing product development costs, potentially jeopardizing eventual product release and availability. This problem can be addressed most effectively by building positive incentives into the license agreement for the licensee to advance the licensed technology itself—e.g., design instrumentation, perform hit-to-lead optimization, file an IND. Such an incentive might be to decrease the percentage of sublicense revenues due to the university as the licensee meets specific milestones.

The details involved in any agreement provisions attempting to address this issue are complex and will require expert planning and careful negotiation. The application will vary in different contexts. The principle, however, is simple. Universities should strive to construct licensing arrangements in ways that ensure that these underprivileged populations have low- or no-cost access to adequate quantities of these medical innovations.

We recognize that licensing initiatives cannot solve the problem by themselves. Licensing techniques alone, without significant added funding, can, at most, enhance access to medicines for which there is demand in wealthier countries. Diseases that afflict only the global poor have long suffered from lack of investment in research and development: the prospects of profit do not exist to draw commercial development, and public funding for diseases suffered by those who live far away from nations that can afford it is difficult to obtain and sustain. Through thoughtful management and licensing of intellectual property, however, drugs, therapies, and agricultural technologies developed at universities can at least help to alleviate suffering from disease or hunger in historically marginalized population groups.

Mr. BERMAN. Dr. Grodman?

TESTIMONY OF MARC GRODMAN, CHAIR OF THE BOARD AND CEO, BIO-REFERENCE LABORATORIES, ELMWOOD PARK, NJ

Dr. GRODMAN. Mr. Chairman, Members of the Subcommittee, I want to thank you for the opportunity to testify on a critical issue of public health.

My name is Marc Grodman. I am a physician as well as founder and CEO of Bio-Reference Laboratories, a publicly traded company. We are the largest independent regional clinical laboratory in the Northeast, employing over 1,700 people with revenues this year that will exceed $250 million. In 2006, Bio-Reference Laboratories purchased Gene Dx, a laboratory in Gaithersburg, Maryland, that does primarily genetic testing. This is an important business opportunity.

Unfortunately, the ability of Gene Dx to offer potentially lifesaving genetic tests have been severely restricted. Gene patent holders have granted exclusive licenses for the testing of genetic disorders, keeping competitors of Gene Dx out, and we think having an adverse effect on the public.

I am not here today to attack the patenting of genes. What I am here to say is that using gene patents for the exclusive licensing of genetic tests for conditions, such as cancer, neurological disease, certain kinds of heart disease, among others, should be severely restricted, if not barred.

A laboratory with an exclusive testing license does not have to compete. It results in substantive quality of the testing as well as excessive pricing, making the test unaffordable to many. It also stifles research innovation. Competition, on the other hand, is the most effective tool we have to address the needs of public health. Let me describe three examples that will explain what I mean.

The first example concerns one of our society's most dangerous killers, breast cancer, and the related breast cancer genes BRCA-1 and BRCA-2. The patent holder has granted an exclusive license to one company to do the diagnostic testing for these genes. Not surprisingly, over the course of time, quality issues arose.

Dr. Chung, from Columbia University, who has submitted testimony along with my testimony, cites in her testimony that for about 10 years the tests of breast cancer genes was not as comprehensive as it might have been, given that there were a number of subsequent mutations that were not found. Competition would never allow this situation to go on, and, in fact, this information is confirmed in the peer-reviewed article, which is also cited in Dr. Chung's testimony.

The second example involves long QT genes that can cause sudden death from heart arrhythmias. These genes were patented and an exclusive license was granted to a single laboratory. For 2 years, the exclusive licensed laboratory went into bankruptcy and no other laboratory could test for this gene.

During this hiatus, Abigail, a 10-year-old child with long QT syndrome, died.

It is not just one or two genes. Each of the genes may mean a different medicine may work. So you really have to do it and do it well, and in that period of time, this girl never had access to the test.

Dr. Chung also describes persistent problems with a test performed by this exclusive laboratory, including long delays in getting results, in determinant findings, high costs, and just the basic lack of improvement by making the test better.

We can make a better test, but under the existing system, we cannot.

The third example is raised by testimony that I submitted from Dr. Kathy Matthews, a child neurologist and pediatrician at the University of Iowa. Dr. Matthews describes serious quality issues that she has encountered with the exclusive licensing of laboratory tests for certain neurological disorders.

It is somewhat amazing that as time goes on and we learn more about the association of different medical conditions and genetic patterns that she is now at a point to where she is referring less.

These scenarios illustrate another problem, that the laboratory with the exclusive license has no incentive to conduct further research, and other laboratories, including academic laboratories, are prevented by the patent holder from doing research as well in many cases.

I believe that competition in diagnostic testing is critical to protecting the public health and, fortunately, is a remedy aside from legislative reform, and that is the Bayh-Dole Act of 1980. This is the act that allows universities to get paid patents on genes even though Federal funds help pay the research. The act, however, recognizes that the patent monopoly obtained through taxpayer funding could be misused.

It specifies specifically a remedy. When the public's health or safety needs are not being reasonably satisfied by the patent holder or its exclusive licensee, the Federal funding agency has the power to march in and provide licenses to other interested parties. Thus, under existing Bayh-Dole legislation, when there are legitimate health and quality complaints about genetic laboratory tests of an exclusive licensee, the NIH may give licenses to other laboratories willing and able to do the tests.

Opening up the licensing process to more than one diagnostic testing laboratory will have a desirable benefit of improvement quality, more research, lower price, and creating a competitive framework at a higher standard by which even the exclusive licensees have to be able to attain.

As a laboratory, we are not seeking any windfall. Under Bayh-Dole, any laboratory given a license through the march-in provisions can and should be charged a reasonable royalty to use the patent.

Even though the NIH has refused to march in in three instances in which it was asked to do so, those cases involved drugs and not gene diagnostic testing and involved issues of price, not efficacy. Therefore, Congress must compel the NIH to enforce the margin provisions of the Bayh-Dole Act.

In conclusion, if we or any company can be able to provide a faster, better, more thorough result, more complete, more efficient tests to the public, the ability to go in and obtain this on a nonexclusive license and then sweep the market will be in the public health's advantage.

Thank you very much.

[The prepared statement of Dr. Grodman follows:]

PREPARED STATEMENT OF MARC GRODMAN

Statement of Dr. Marc Grodman,
CEO of Bio-Reference Laboratories, Inc.

The House Judiciary Subcommittee on Courts, the Internet and Intellectual Property in Connection with its hearing on "Stifling or Stimulating - The Role of Gene Patents in Research and Genetic Testing"

October 30, 2007

Mr. Chairman, members of the subcommittee, I want to thank you for the opportunity of testifying on a critical issue public health. I also want to congratulate the subcommittee for its leadership in scheduling this hearing on the important topic of the impact of gene patenting n genetic testing.

My name is Marc Grodman. I am the founder and CEO of Bio-Reference Laboratories (BRLI), a publicly traded company with headquarters in Elmwood Park, New Jersey that is the largest independent regional clinical laboratory in the Northeast, as well as providing national service in certain specialized areas. For almost 25 I have also been an attending physician on the medical wards of Columbia University's College of Physicians and Surgeons' New York-Presbyterian Hospital.

BRLI is a full service clinical laboratory. This means that we analyze blood, urine and tissue samples for a whole host of conditions, including diabetes, HIV/AIDS and hepatitis, to name a few. We have specialty capabilities in the areas of oncology and genetics. We employ almost 1700 individuals and serve physicians across the country who send us the samples to test. Over the past twenty years, BRLI has grown substantially. This year its revenues will total more than a quarter of a billion dollars, up from a two hundred thousand dollars in 1987.

A few years ago, I was making rounds with the interns when a patient was presented whose heart muscle was defective. She had a condition known as hypertrophic cardiomyopathy. A significant number of people with this condition are susceptible to sudden death syndrome. I asked the medical student to tell me the options for treating this patient and discovered for the first time that we could diagnose the condition by using a genetic test. In the past, our ability to make an exact diagnosis was limited; using data from an EKG and evaluating the shape of the heart using an echocardiogram, we hoped to have clues to the severity of the condition. But, as I learned at that time, with proper genetic testing, a much more accurate diagnosis could be made and the risk of sudden death could be properly evaluated and even reduced. That impressed me.

At the outset, I want to make it clear that that I am not here to attack the entire U.S. patent system, or even the patenting of genes or gene sequences *per se*. I am also not here to challenge the rights of universities under the Bayh-Dole Act of 1980 ("Bayh-Dole") to profit from the commercialization of their discoveries. While historically, patents, which confer legal monopolies of limited duration, have benefited society in numerous ways, such as by increasing innovation, in the case of genetic diagnostic testing that is patent protected and exclusively licensed the public health has been adversely affected. What I am saying is that the exclusive licensing of genetic associations, meaning of specific gene sequences or mutations in relation to certain clinical conditions, should be barred.

I would like to focus my remarks on two points: (1) explaining how the grant of exclusive patent licenses for conducting genetic diagnostic tests runs contrary to the public health; and (2) proposing a practical and simple remedy for this problem, which involves the Bayh-Dole Act of 1980.

I became personally familiar with the issues when in 2006, BRLI purchased GeneDx, a wonderful laboratory, not far from here in Gaithersburg, Maryland, that does DNA sequencing, analyzing each base pair of the chromosomes, to diagnosis rare genetic disorders. In addition to diagnosing genetic disease outright, GeneDx has the ability to test for human genes that are associated with certain diseases or that make a person highly susceptible to a certain disease. My company was excited by the opportunity to participate in the forefront of modern medicine and at the same time take advantage of an important business opportunity.

Unfortunately, however, the ability of GeneDx to offer these genetic tests has been severely restricted by gene patent holders or their exclusive licensees, such that GeneDx, as well as other clinical laboratories, may not provide tests without the threat of being sued for infringing gene-related patent.

How has this problem arisen?

The patent holder of a gene patent, usually a university where the original research was conducted, controls the commercial use of the gene. This means that a laboratory cannot analyze the gene for mutations in order to diagnose the presence of a disease or condition, such as breast cancer or muscular dystrophy, without permission of the patent holder. In cases where the university grants licenses to multiple laboratories to conduct the diagnostic tests, the public interest and technological advancement are generally promoted through the competitive process.

Indeed many institutions, including the National Institutes of Health (NIH), major universities, and the Association of University Technology Managers (AUTM) believe that the best practice is to limit strictly the grant of exclusive licenses to extraordinary circumstances.

More particularly, the NIH recommended policy is to restrict the licensing of genomic inventions to non-exclusive approaches "whenever possible." A non-exclusive licensing approach "whenever possible" favors and facilitates making broad enabling technologies and research uses of inventions widely available and accessible to the scientific community. See, "Best Practices for the Licensing of Genomic Inventions: Final Notice" (70 Fed. Reg. 18413, 18415, April 11, 2005), at http://www.ott.nih.gov/pdfs/70FR18413.pdf (last visited October 25, 2007).

Similarly, AUTM recently came out with their recommendation of a consensus recommendation by about a dozen major U.S. research universities entitled "In the Public Interest: Nine Points to Consider in Licensing University Technology." This policy, published on March 6, 2007 addresses the need for commercial arrangements to be cognizant of the public good. http://www.autm.net/ninepoints_endorsement.cfm, last visited October 26, 2007.

I have to confess to a strong underlying belief—competition in diagnostic testing is critical to protection the public health. Right now, except when blocked by exclusive licenses, clinical laboratories compete. We compete on service—getting back the results in a timely manner and in a way that contains clinically useful information to the physician and perhaps the patient. We compete on quality—we have to get the right result; if we do not, then we will suffer the consequences – the loss of business. We compete on price--we know if we are more efficient we can get more business. We need to compete fully and across the board on technology. We need, for example, to be able see if there is one area of the human genome that has been associated with one condition or disease might have new or further meaning when combined with another area of the human genome. This robust competition protects the public. When a gene is the exclusive province of a single laboratory because of an exclusive licensing agreement, that laboratory does not have to compete on any of these factors. The absence of competition leads to substandard quality of tests, inadequate marketing of or information about tests, as well as to excessive pricing, making the tests unaffordable and unavailable to thousands of individuals.

Let me give you several examples of the problems my laboratory has encountered in trying to do its business. In one case, shortly after we acquired GeneDx, one of our customers, a geneticist, asked for a diagnosis for a rare skin disorder. While we were in the process of sequencing the gene in order to make a diagnosis, we received a letter from another laboratory claiming that within the sequence we were analyzing was another sequence associated with hearing loss. We were told that this hearing loss area was patent protected and that we could not proceed further without infringing the patent. The laboratory would not accept a fee or royalty from us to conduct the genetic test, but said that the patient would have to submit DNA to them for testing; they would just re-do our existing work at full cost to the patient to confirm what we had already done.

We have experienced another notable example of the problem involving genes associated with Long QT Syndrome. Long QT Syndrome is a disorder of the heart's electrical system that is characterized by irregular heart rhythms and risk of sudden death. The discovery of these genes was partially funded by the NIH. Numerous U.S. patents were obtained on the genes and the patent holder (the University of Utah) granted an exclusive license to one laboratory to develop and offer the diagnostic test for the genes.

We have consulted with Dr. Wendy Chung, a highly respected physician and research scientist at Columbia University's New York-Presbyterian Hospital, who has informed us that there have been serious quality problems which continue, generally unresolved, in connection with the LQT Syndrome tests. A key problem relates to inaccurate or incomplete testing. Thus, tests done by the exclusively licensed clinical laboratory failed to detect mutations that were found in the same patients Dr. Chung's research laboratory. One such case involved a five year old child who was at very high risk of sudden cardiac death. An incorrect test could have had fatal consequences for the child. An incorrect diagnosis in the child would also have left over 20 other mutation carriers in her family at risk for sudden cardiac death. A system that allows only one laboratory to conduct a genetic test creates other problems as well. Dr. Chung has also informed us that the turn around time for the test is lengthy, and can take as long as six to eight weeks. Finally, the price of the test to the public is currently $5,400 even though a competitive laboratory could offer the test for about a quarter of the price. I am submitting as Appendix A to the subcommittee a written statement by Dr. Chung that describes in greater detail the problems with the Long QT syndrome test.

The University of Utah awarded an exclusive license to DNA Sciences for genetic testing in several genes associated with LQT. However, DNA Sciences never developed a genetic test for this disorder. Meanwhile, GeneDx *did* develop testing and made it available to the public. DNA Sciences sued GeneDx for infringement, and would not issue GeneDx a sub-license to offer testing. DNASciences was sold to another company. GeneDx contacted the new company and requested a license. The new company refused. GeneDx asked simply to be allowed to offer the test only so long as the new company was getting their test ready, so that there would be testing available to the patients and their families in the interim. The new company refused. The new company was then purchased by yet another company. Thus there was a full 2-year period during which genetic testing was not available for this disorder which kills children and young adults. I am aware of at least one patient, Abigail, who during this time developed an arrythmia. If testing were available, the cause of Abigail's arrythmia would have been diagnosed and the correct therapy been instituted. However, Abigail died suddenly at age 10 from her undiagnosed LQT syndrome.

In sum, we have tried, with no success, to sublicense the Long QT genes from the laboratory with the exclusive patent rights so that we could offer the test to the public. I am convinced that if we had the rights to perform this test, we could do a better job and do it less expensively so that the test would be more widely available.

This problem extends to many other genetic diseases aside from LQT genes. One well-publicized example of this problem has to do with BRCA1/BRCA2, the genes whose mutation results in a predisposition to breast cancer, ovarian cancer and even prostate cancer. These genes were also discovered with the help of funding from the National Institutes of Health. There are multiple patents in this portfolio, including many owned or co-owned by the University of Utah. The University of Utah has granted an exclusive license to its owned or co-owned patents to one company to develop, use and commercialize the diagnostic tests for BRCA1 and BRCA2.

To begin with, there were several problems with the BRCA1 and BRCA2 tests, according to information we have received from Dr. Chung , which is contained in her statement to the subcommittee. For example, for many years, the testing procedures did not include genomic deletions and rearrangements. As a result, there were a number of mutations that were not detected by the test offered until 2006, meaning that the tests were not as comprehensive as they could have been if other companies and researchers had been permitted to create a better test. Furthermore, the laboratory's insistence on testing blood only has restricted the test unnecessarily in instances in which there is no blood but only other genetic material. The cost of the test, which is still high--approximately $3,000-- poses a problem for people who are uninsured or live in states in which Medicaid does not reimburse the cost.

In addition to BRCA1 and 2 and Long QT Syndrome genes, many providers have discontinued or have been prevented from providing genetic testing for other diseases. I am submitting as Appendix B to the subcommittee a statement provided to me by Dr. Katherine Matthews, a neurological pediatrician at the University of Iowa, describing the serious problems she has encountered previously with the exclusive licensing of gene patents in the area of neurological disorders. Many of these problems are similar to those described by Dr. Chung in her statement.

It is my strong belief that the exclusive licensing of genetic diagnostic patents is creating a serious public health problem. As the number of genes that are discovered to be associated in some manner to a certain disease keeps increasing, so will the problems. It is clear that while the function of many genes has already been discovered, many correlations between mutations in these genes and diseases still remain to be discovered. I expect that such discoveries will accelerate in the next few years, and that the number of established correlations will grow exponentially. And, since the numbers of discovered genetic correlations will grow, so will the numbers of patents and the number of exclusive licenses for diagnostic tests.

There is another significant problem caused by exclusive licenses: innovation is stifled. As Dr. Chung's statement demonstrates when an exclusive license is granted research on finding new genes which will enhance the clinical significance of the original discovery is brought to a halt.

I do not have a problem if the discoverers of such correlations obtain patent protection for the diagnostic applications of these correlations. I understand that the research enterprise needs financing and involves risks. Patent protection is a time proven method of trying to control such risks. In the case of genetic diagnostic correlations, however, it is my view that the risks are not as high nor the uncertainties as deep as is the case in the discovery of new drugs. I know that getting a new drug from discovery all the way through approval by the FDA may cost up to or more than $1 billion and involve a decade or more of work and uncertainty. Exclusive patent protection is critical in order to fund such endeavors.

In contrast, in the case of the discovery of genetic correlations to diagnosing disease or disease predisposition, the investment in time and money, the uncertainty, and the regulatory hurdles are not nearly as onerous as in the case of drugs. For example, a service laboratory like my company could enter the market quickly at only a small fraction of the cost of what would be needed in the pharmaceutical industry. Allowing companies like mine, that can put a diagnostic test on the market and provide competition to other laboratories in the same area, will be extremely beneficial to the public health.

I am therefore in favor of a regime where a company like mine can obtain a non-exclusive license from the holder of the patent or obtain a non-exclusive sublicense from the licensee of the patent. If I can demonstrate that my test would be better, faster, provide fewer false negatives or positives, fill a niche, cost less to the public or perhaps complement the test already offered by my competitor then the public will benefit greatly by my entry. I am not asking for a free ride; all I am asking for is the ability to compete fairly and benefit the public and my company.

In the area of genetic testing, exclusivity is a formula for mediocrity.

Fortunately, I believe that the Bayh-Dole Act of 1980 offers a ready solution to these problems that requires no legislation at all.

The Bayh-Dole Act was enacted more than twenty years ago to encourage the commercialization of patents obtained through federal funding by allowing the universities sponsoring the research to hold the patent. Nonetheless, Congress understood that this patent monopoly, based on taxpayer funding, could be misused--and Congress specified a remedy for the misuse. Thus, the Act empowers the federal agency financing the research to "march in"--and provide licenses to other interested parties--when, for example, the "health or safety needs" of the American people are not being "reasonably satisfied" by the patent holder or its exclusive licensee.

The march-in rights are clearly spelled out in Bayh-Dole (35 U.S.C. § 203 (a)(2)):

> (a) With respect to any subject invention in which a small business firm or nonprofit organization [e.g. a university] has acquired title under this chapter, the Federal agency under whose funding agreement the subject invention was made [e.g. NIH] shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder, to require the contractor, an assignee, or exclusive licensee of a subject invention [e.g. in the case of the Long QT exclusive licensee] to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such
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> (2) action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees...

Bayh-Dole applies because most of the research leading to gene patents have been funded by the federal government.

I am aware that the NIH has never exercised its "march in" powers. I also know that it has denied three formal requests to "march in," although none of those instances involved diagnostic genetic tests.

In its opinions on two of those requests (Norvir™, manufactured by Abbott Laboratories, decided July 29, 2004; and Xalatan™, manufactured by Pfizer, decided September 17, 2004), the NIH indicated that the cases rested essentially on complaints about pricing alone, and asserted that "march in" rights were not designed for "controlling" drug prices. In addition, because in both instances the FDA had approved the drugs as safe and effective and no evidence had been presented by the requesters that march-in would alleviate health or safety needs not met by Abbott or Pfizer, the NIH declined to act. As I will demonstrate below the situation with genetic diagnostic tests is entirely different from that of these drugs.

The third denied request involved a 1997 petition from Baxter Labs that the NIH initiate march-in proceedings in a litigation between two competing products for separating stem cells. See, *Johns Hopkins University v Cellpro Inc.,* 152 F3d 1342(Fed. Cir., 1998). The NIH found no health and safety needs at issue because the difference between the products was just one of "convenience of use." The NIH found that Baxter had taken appropriate steps to reasonably satisfy "health or safety needs," and did not initiate proceedings.

None of these cases, I believe, poses any obstacle to NIH's use of "march in" powers to ensure that the public's "health and safety needs" are met by diagnostic genetic laboratory tests. In fact, the exercise of march-in rights would be especially appropriate in cases involving diagnostic gene testing, wider availability and incidentally, lower cost to the public.

There is a fundamental difference between the situation of drug companies and diagnostic laboratories, as I have pointed out previously. Given the huge costs of drug development, breaking up exclusive patent rights for drugs could have serious consequences for the willingness of companies to undertake the needed research in the first place. Without solid patent protection, the companies could see no way to recoup their enormous investment. But in the area of gene patents for diagnostic tests, efforts to identify new genes and their correlation with disease would not seriously be discouraged by the absence of exclusive patent rights for several reasons. The costs of discovery are not comparable to those for drug development. Furthermore, because there are other ways of gaining royalties from the gene identification--for example development of drugs for the diseases themselves--the loss of some royalties from non exclusivity on lab tests is not likely to have a serious adverse impact on the incentives to identification.

Another major difference between drugs and genetic diagnostic tests is found in the very nature of the two technologies. In the case where a drug is patented by one pharmaceutical company, its competitors are not prevented from continuing their research into the same disease with the expectation that they can develop different drugs that will avoid the patent holder's patent. The disease itself is not patented, as it obviously cannot be since it is a natural phenomenon. Thus, there are a potentially unlimited number of drugs of different compositions and structures that might be tested and proposed for treating the same disease. In genetic diagnostics, in contrast, for a given disease such as Long QT Syndrome, we are dealing with one or at most a handful of genes and their correlations. Once these are in exclusive hands for the average life of a patent, say 18 years, neither I nor others can enter the field and use the patented genes to find other genes or improve the tests that correlate to the same disease. In fact, since my work is primarily commercial in nature, were my researchers to do commercially relevant discovery research with patented genes, I understand that such research would constitute patent infringement of the rights of the exclusive holder. See, *Roche Products Inc., v. Bolar Pharmaceutical Co. Inc.*, 733 F2d 858 (Fed. Cir. 1984). The public does not benefit from such a situation.

In addition, breaking up exclusive licenses need not provide a windfall for my company or any other company. The Bayh-Dole section of the patent law contemplates expressly that the marching-in agency arrange that a license or sublicense be given to a responsible applicant "upon terms that are reasonable under the circumstances." See 35 U.S.C. 202(a). This clearly envisions the calculation of a reasonable royalty – not a royalty free license. There is plenty of precedent for reasonable royalties in other areas of the patent law, such as 35 U.S.C. 154 (a "reasonable royalty" to be charged to a party who has been on notice of pending patent claims that later issue) and 25 U.S.C. 284 (after losing an infringement lawsuit the infringer has to pay damages no less that a "reasonable royalty"). The courts have developed a lengthy jurisprudence on what is a "reasonable royalty" for damages for patent infringement. See for example *Georgia-Pacific Corp. v. U.S. Plywood Corp.*, 318 F. Supp. 1116 (S.D.N.Y. 1970) (using 15 factors to determine a "reasonable royalty" such as the nature of the invention, other established royalties for the same patent, other comparable royalties, the custom of the industry, etc.).

Finally, calculating reasonable royalties is a well known exercise to patent-savvy universities and to the NIH's Office of Technology Transfer, both of which have licensed out their own extensive portfolios of patents in the last few decades.

Bayh-Dole vested the government with the responsibility of ensuring that government funded technology licenses protect the best interests of the public. In light of the foregoing, I believe that this committee should require that the that NIH enforce the "march in" provisions of Bayh-Dole in appropriate cases involving diagnostic genetic testing, including the ones outlined above. This is a feasible and indeed necessary way to ensure that the public's health and safety needs are met more widely with regard to DNA diagnostic and susceptibility testing. If the NIH is unwilling or unable to enforce the law as written, then Congress should review whether the power to enforce Bayh Dole should be placed in the hands of another federal agency. The NIH cannot be permitted to let Bayh Dole's march in provisions become dead letter law. The NIH must implement the law, not nullify it.

I have deliberately not discussed in detail other obvious remedies. The subcommittee is clearly aware that there are legislative solutions, such as the bill that was proposed by former Rep. Lynn Rivers. In my opinion, there is no need for a study to document further a problem that is already well known in the field of genetic diagnostic testing.

I have valued this opportunity to share my views on the serious public health consequences of exclusive patents for diagnostic gene testing. I most respectfully urge the subcommittee to adopt a remedy promptly to the problem I have described.

Appendix A

Statement of Dr. Wendy Chung
Submitted in Connection with the Statement of Dr. Marc Grodman,
CEO of Bio-Reference Laboratories, Inc.

The House Judiciary Subcommittee on Courts, the Internet and Intellectual Property in connection with a hearing on Stifling or Stimulating - The Role of Gene Patents in Research and Genetic Testing

October 25, 2007

Mr. Chairman, Members of the Subcommittee,

Thank you very much for the opportunity to submit this statement which accompanies the Statement submitted by Dr. Marc Grodman, CEO of Bio-Reference Laboratories, Inc.

My name is Wendy Chung, MD, PhD. I am a clinical and molecular geneticist and am director of Clinical Genetics at Columbia University. I am director of the fellowship program in molecular genetics and cytogenetics at Columbia University and direct both a clinical and research molecular genetics laboratory. I am the Herbert Irving assistant professor of pediatrics and medicine at Columbia University. I have been conducting research in human genetics for the last 17 years in the areas of obesity, diabetes, breast cancer, pulmonary hypertension, inherited arrhythmias, congenital heart disease, and spinal muscular atrophy.

In recent years, there has been groundbreaking research in human genetics that has identified the genetic basis for over 2200 human diseases. Genes have been identified for nearly all types of human disease including susceptibility to breast cancer, colon cancer, Parkinson disease, Alzheimer's disease, stroke, coronary artery disease and myocardial infarction, arrhythmias, diabetes, and macular degeneration. These conditions are not rare diseases, but are common conditions from which the majority of Americans will suffer at some point in their lives. Importantly, for many of these conditions, there are effective preventive measures that can be taken if patients know they are at risk. Therefore, genetic testing for these conditions plays a crucial role in allowing patients to assess diseases for which they are at risk, quantify the level of risk, and determine the interventions that will be most effective given the molecular basis of their disease predisposition.

Clinical testing is now available for over 1180 of these genetic disorders, but in approximately 20% of these cases, only one laboratory is available to perform such testing, and genetic testing is often expensive ($1000-$5400) with long turn around times (approximately 2 months), and often ambiguous results. The provision of inexpensive, clinically useful genetic testing has been stifled in part based upon the issuance of patents for genes and provision of exclusive licenses that allow only a single laboratory to perform clinical genetic testing.

As significant as our previous advances in human genetics have been, within the last year alone, there has been an explosion in the identification of multiple genetic risk factors for many more diseases including inflammatory bowel disease, myocardial infarction, asthma, diabetes, and obesity. These advances were made using a genetic technique called genome wide association studies which will likely continue to identify many additional genetic risk factors for common diseases. To continue translating these genetic discoveries into improved health and quality of life, it is critical to ensure that affordable, interpretable clinical genetic tests will be available to all Americans.

A significant obstacle to providing this effective genetic testing to patients has been the issuance of patents on human genes and the issuance of exclusive licenses to use these genes for diagnostic purposes to a single laboratory. Neither one alone, but issuance of BOTH gene patents AND exclusive licenses in combination result in a monopoly in the provision of genetic tests. It should be noted that the majority of genes for human diseases do not have both gene patents and exclusive licenses granted for genetic testing. However, there are a few notable examples for which this has occurred that have had detrimental results for the public good which we will discuss below.

Many of the genes for human diseases have been discovered in part or in whole in laboratories within universities and medical schools, funded in large part by the National Institutes of Health. Under this system, the patent holder controls the commercial use of the gene. In many cases where the university or medical school grants licenses to multiple companies, the public interest and technological advancement are promoted through the competitive marketplace. In those cases, however, where the patent holder on the gene grants an exclusive license to a single laboratory to develop and market diagnostic tests for that gene, the monopoly on the test generally leads to unfavorable consequences. The resulting monopoly in genetic diagnostic testing has many of the same effects as monopolies in other sectors. If there is only a single provider for a medical genetic testing, there is no competition or market force. This leads to substandard quality of the tests, inability for physicians to independently confirm a test result, lack of innovation and test improvement, slow turn around times for testing, and excessively high prices that often make these tests unavailable to many patients and unnecessarily increases the cost of health care provision by third party payers.

There are two especially noteworthy examples of this problem with gene patents and exclusive licenses.

The first example is for hereditary breast and ovarian cancer due to mutations in BRCA1 and BRCA2, the research on which was partially funded by the NIH. As the patent holder, the company refused to issue licenses to any other laboratories, commercial or academic, to provide a comprehensive diagnostic test for BRCA1 and BRCA2. That company had relied exclusively upon sequencing technology for 10 years to screen for mutations in these genes, a technology that is expensive and able to detect some but not all mutations in these genes. Large deletions, insertions, and re-arrangements in BRCA1/BRCA2 cannot be detected by this methodology and were known to be a cause of mutations (Walsh *et al. JAMA 295*: 1379, 2006). It was only after considerable pressure from the scientific community that the company added methods to detect these deletions, insertions, and re-arrangements in 2006, over 10 years after they first introduced clinical genetic testing, and barred anyone else from performing the tests. In a competitive marketplace, this delay never would have occurred.

Test result interpretation provided by the company has been problematic. As of 2005, approximately 1433 BRCA1/BRCA2 genetic tests had been reported out by the company to have "variants of unknown significance" which leaves the patient and the physician not knowing whether or not the patient is at increased risk for breast and/or ovarian cancer. Many patients not knowing how to interpret this information, yet fearing cancer in their future, have had prophylactic oophorectomies and mastectomies assuming that this test result means that they are at substantially increased risk for breast and/or ovarian cancer. Given that the vast majority of these variants of unknown significance are benign, many of these women who chose to have the prophylactic surgery were probably not at increased risk for one or both of these cancers. These variants of unknown significance are reported disproportionately in minority populations

(African Americans, Hispanics, and Asians) because we have less information about the normal genetic variation in minority populations who are less likely to participate in research studies unless diagnostic laboratories proactively gather this information. Rather than developing the necessary databases of normal genetic variants in multiple ethnic groups, scientifically analyzing the conservation of these nucleotide positions across other species, correlating these variants with the personal and family histories of the patients tested, and/or performing biological assays to functionally assess these variants, the company simply continues to report out ambiguous results because there is no incentive for them to improve the quality of the data interpretation since they face no competition in the market. Furthermore, until recently, all these data were held exclusively by the company so there was no ability for scientists to conduct these experiments themselves for the benefit of the public.

The company is willing to perform genetic testing only on blood samples and has not developed the ability to perform genetic testing on paraffin embedded tissue from previous cancer specimens although this testing is routinely performed in research laboratories. In many cases, the family member with either breast or ovarian cancer is deceased and the only source of genetic material for testing is a tumor sample that was previously removed. Testing an affected family member is necessary for accurate interpretation of a negative result in other unaffected family members. A negative genetic result in the daughter of a BRCA1 or BRCA2 mutation carrier reduces the daughter's risk of cancer to that of the general population while the cancer risk for a daughter with a negative genetic result of a mother who had early onset breast cancer but was negative for BRCA1 or BRCA2 remains substantially elevated over the general population. Again, without competition, the company has had no incentive to develop genetic testing from sources other than blood, cruelly leaving families at risk with no remedy.

The cost of BRCA1/BRCA2 testing has remained substantial, costing approximately $3000 from the time it was first offered 12 years ago. The cost could have been reduced by offering targeted rather than comprehensive testing for specific populations in which founder mutations account for a large fraction of all mutations. This has been offered for Ashkenazi Jews in the US, but for no other populations. For the first seven years, many insurance companies did not cover genetic testing for BRCA1/BRCA2 or required a lengthy preauthorization process that discouraged many patients from pursuing testing. Some of my patients died during that preauthorization process, and then the families were not able to get their affected family member tested to guide their future medical care. In addition, for the first eight years, the testing was not covered by Medicare, and for the first ten years and still in many states is not covered by Medicaid. This has created enormous disparities in access to the BRCA1/BRCA2 diagnostic tests due to the high cost which has continued to increase over the years to the current cost of $3200.

The second notable example has been for genetic testing for Long QT Syndrome which is associated with fatal arrhythmias of the heart and sudden death. These results can be prevented by avoiding triggers such as heart rates that are too fast or too slow or startling sounds during sleep, taking medication, and having a cardiac defibrillator implanted. Importantly, the therapy for each patient is based upon his or her molecular genetic defect. There are now 9 molecular subtypes of Long QT syndrome, and the triggers for arrhythmias and the most appropriate medical therapy depends upon which gene is mutated, a fact that can only be determined by genetic testing. A medication that is commonly used for Long QT syndrome, beta blockers, which decrease the heart rate, are the first line drug for Long QT1 and Long QT2, but actually increase the risk of arrhythmias in Long QT3 which is more appropriately treated with medications such as mexiletine or flecainide.

The discovery of these genes for Long QT syndrome was partially funded by the National Institutes of Health. Patents were obtained on many of the first Long QT genes by the University of Utah, which granted an exclusive license to one laboratory to develop and provide a diagnostic test for the genes. DNA Sciences, the first commercial laboratory to offer testing, forced two other laboratories to cease and desist offering genetic testing for Long QT syndrome on the basis of their exclusive licenses. DNA Sciences subsequently went out of business, and for a period of time patients were unable to get any genetic testing for Long QT syndrome because the license holder was not performing testing. The licenses were subsequently purchased by Clinical Data Systems which is again the only laboratory licensed to offer genetic testing for Long QT syndrome. Many of the same problems that the medical community has experienced with BRCA1/BRCA2 testing have been repeated with Long QT syndrome testing because there is a monopoly on the testing. I describe them below.

Although the number of genes for Long QT syndrome has increased from 5 to 9 over the time that clinical testing has been made available, there has been no increase in the number of genes analyzed by the exclusively licensed laboratory, even though this would improve the testing sensitivity and would be clinically important.

Most concerning is that the company has rendered genetic testing results to me that have several times been inconsistent with independent genetic data obtained in my laboratory For most patients there is no ability to independently confirm these results since there is no other clinical laboratory performing this testing., There are instances where I have independently performed genetic testing in my research laboratory and then sent samples to the company for independent confirmation prior to initiating medical therapy based upon their genetic test results and then found inconsistencies. One case would have had devastating effects for a 5 year old patient and her family since she carries two mutations (usually only one mutation is necessary for Long QT syndrome) and has a particularly malignant form of Long QT syndrome associated with nearly 100% mortality in childhood without intervention. Furthermore, because the mutation was inherited from both her mother and father, 20 other mutation carriers in her family are at risk for sudden cardiac death would have been missed had we not independently confirmed the correct result. In a competitive environment, where there is another laboratory offering this test, this situation would never exist. That company has also incorrectly reported genetic variants as disease associated because they have misinterpreted the scientific literature. There are many Long QT genetic variants that are associated with prolongation of the QT interval only upon exposure to certain medications that prolong the QT interval, but otherwise do not cause problems if patients do not take medications that prolong the QT interval. Patients carrying these variants should avoid such medications that prolong the QT interval, but do not have a high risk of sudden cardiac death if they do not take these medications. The company also reports some of these drug induced Long QT variants as independent Long QT mutations, leading many cardiologists to pursue overly aggressive intervention with medication and implantable defibrillators.

Similar to genetic testing for BRCA1/BRCA2, the company reports out "Class II variants of unknown significance" in approximately 5% of their test reports. These variants of unknown significance are reported disproportionately in minority populations (African Americans, Hispanics, and Asians) and is often extremely anxiety provoking and often leads to prophylactic implantation of a defibrillator. Rather than developing the necessary databases of normal genetic variants in multiple ethnic groups, scientifically analyzing the conservation of these nucleotide positions across other species, correlating these variants with the personal and family histories of the patients tested, and/or performing biological assays to functionally assess these variants, the company has not improved the test interpretation. Furthermore, the database of genetic variants is not publicly available, so there is no opportunity for scientists and physicians to attempt to interpret the genetic test results themselves beyond the information they have on their patient and the information in the scientific literature, leaving patients and physicians wondering if the patient really has Long QT syndrome or what treatment would be beneficial. Plainly, the exclusive license stifles scientific research and creates a barrier to medical progress.

The company is only willing to perform genetic testing on blood samples and has not developed the ability to perform genetic testing on paraffin embedded tissue tissues although this testing is routinely performed in research laboratories. Unfortunately, many of the cases that require testing are cases of sudden death, particularly sudden infant death syndrome (SIDS) in which the autopsy is normal. In such cases, usually the only tissue available for testing after the autopsy is paraffin embedded tissue. For families to obtain closure on the cause of death of their loved one and prevent similar deaths in other family members, it would be important to be able to perform genetic testing on fixed tissues.

The current cost of genetic testing for Long QT syndrome is $5,400 and is not routinely covered by most insurance companies without a lengthy preauthorization process that frequently takes 3-12 months to complete. Furthermore, testing is not covered at all by Medicare or Medicaid. The actual cost of the testing without the cost of the licensing fees could be 25% or less of the existing price and would be accessible to many more patients if it were correctly priced in a competitive market.

In summary, when genetic testing is performed by a single laboratory, the quality of the genetic testing and interpretation of results suffer, and the price of the testing remains artificially elevated to the detriment of patients who could take preventive measures to preserve their health if provided with accurate information to determine their risk of life threatening diseases.

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Appendix B

Statement of Dr. Katherine Mathews

Submitted in Connection with the Statement of Dr. Marc Grodman, CEO of Bio-reference Laboratories, Inc.

Before the House Judiciary Subcommittee on Courts, the Internet and Intellectual Property

"Stifling of Stimulating – The Role of Gene Patents in research and Genetic Testing"

Dated: October 26, 2007

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Mr. Chairman, Members of the Subcommittee,

Thank you very much for the opportunity to submit this statement which accompanies the Statement submitted by Dr. Marc Grodman, CEO of Bio-reference Laboratories, Inc. My purpose in submitting testimony today is to provide first hand information about how the lack of competition among clinical laboratories offering specific genetic tests affects the quality of care that patients receive. I hope that my testimony will help in your consideration of questions concerning the role of gene patents in genetic testing.

I am a pediatric neurologist with expertise in neurogenetics and neuromuscular disease. In my clinical practice, genetic testing is often the most efficient, cost effective and/or accurate way to make a specific diagnosis. There is a choice of laboratories that offer the testing for some of these genetic tests. In this case, the University of Iowa Pathology Department has worked with clinicians such as me to choose the laboratories that provide the best service, most accurate and thoughtful results and are most cost effective. (This is also our approach to choosing reference laboratories for non-genetic diagnostic tests.) However, as you have heard, other genetic tests are available from a single commercial laboratory which has exclusive rights to the use of that gene in clinical testing. If a single laboratory has excessive costs, poor service or consistently inaccurate or incomplete results, I have few options. I can cease to offer the genetic test to my patients, or I can continue to accept suboptimal information for those patients who can afford the testing.

In my own case, after experiencing a consistent and unremitting pattern of laboratory and administrative errors that negatively impacted my care for patients, and after hours on the phone trying to correct or identify the basis of the problems, I notified one laboratory in writing in 2005 that I would no longer be sending them samples for one type of disease. Unfortunately, because the laboratory in question has exclusive rights to the testing for this disease and other diseases I deal with commonly, I have had to continue using them on occasion, and the problems have continued. In my management of a patient with one of these diseases, whenever I feel that not making a specific genetic diagnosis is a medically acceptable option, I explain to the patient that the only source of genetic testing has been unreliable and difficult to work with in my experience. Therefore I recommend that we forgo genetic testing at this time.

I will attempt to outline the problems that have led to this approach and present some typical examples.

Case 1.
This case (and several others presented here) involves inherited peripheral neuropathy, or Charcot-Marie-Tooth disease. Neuropathies are caused by loss of function of the nerves going to the limbs and typically result in weakness of the ankles, lower legs and hands; absent reflexes; and decreased sensation in the feet and hands. There are many reasons a person might have neuropathy (such as diabetes). One subset of the neuropathies is inherited and there is an ever-increasing list of specific genes that are associated with inherited neuropathies. The inherited neuropathies as a group are called Charcot-Marie-Tooth disease, or CMT, and each genetic cause is given a specific number/letter designation, such as Charcot-Marie-Tooth type 1A, CMT1A. It is often helpful to make a specific genetic diagnosis to allow accurate genetic counseling to a family as the different subtypes are inherited differently (illustrated in Case 4 below). Arriving at a specific genetic diagnosis also prevents unnecessary, expensive and sometimes painful testing looking for other, non-genetic causes of neuropathy.

An adopted child was referred for increased falling and the physical findings indicated this was likely a neuropathy. She also had several other medical problems, making the diagnosis more complex. The most common reason for a child to have a neuropathy is that it is inherited (CMT as discussed above). I ordered genetic testing for CMT1A, the most common form of CMT. The test was called "not interpretable" and a second sample was requested. One month after the first sample, the second was sent. Five months after the original test and 4 months after the second, after several phone calls from the family asking about the results and numerous phone calls to the laboratory, the report was released. The diagnosis of CMT 1A was highly likely. This whole process was surprising, as genetic testing for this disease has been available for more than 10 years, many laboratories used to offer the testing (before the exclusivity restrictions were enforced), and interpretation of test results is usually extremely straightforward and available within 2 weeks (which is what the family had been told by me).

In phone calls with this lab, we were told that the reason for the difficulty with this case was that the laboratory had recently changed the way they performed the test, and were finding a small number of patients (such as this one) whose results they had not expected. The laboratory didn't have a back up approach in place to assist with interpretation (such as repeating the test, using the previous or one of several other possible technologies) and apparently had not tested this technique to identify such potential problems prior to implementing the change clinically. Furthermore, the several month delay before the lab director would complete the report suggests that the lab director lacked sufficient understanding of the genetics of this disease to interpret the results. Finally, the lab director did not appear to have contacted an expert in the field for assistance. This case left the family involved very unhappy, and gave me very little confidence in the laboratory.

Case 2.
A 47 year old woman and her adult children were referred for genetic counseling. She has progressive ataxia (unsteady gait) resulting in significant disability, as do many of her family members. The clinical diagnosis is spinocerebellar ataxia (SCA) and there are more than 20 different genetic causes of SCA. The different genetic causes are clinically indistinguishable, so genetic testing is required for a specific diagnosis. This patient had genetic testing done by a previous neurologist. The report showed that most of the SCA genes were normal, and one (SCA8) was interpreted as "borderline". The report states that it could not be determined if this borderline result was associated with disease. However, the objective results (as opposed to the interpretation) of the genetic testing for this patient were also listed. The SCA8 result was 99; with normal being up to 50 in the literature, and up to 70 in this lab's own report. Clearly, 99 was in an abnormal range rather than a borderline range. There was no explanation for this discrepancy in the comments or interpretation of the report. This information is critical to provide accurate counseling to the children of the patient. Therefore, the neuromuscular nurse called the lab, where the director agreed that the interpretation did not make sense. The lab requested a second sample, which they will test at no charge to clarify the diagnosis. (Results are still pending.)

While the response to our concerns was very appropriate and helpful in this instance, errors in interpretation of this magnitude are outside of what is expected for a clinical laboratory. Most physicians only read the "Interpretation" section of a genetic test report. They rely on the expertise and knowledge of the laboratory director.

Case 3.
This case was sent to me by a colleague at a different university. A great deal of detail was included in the summary and I was told that the entire situation is documented in the medical record. This case involves a disease called CADASIL that typically causes strokes and migraines in young adults. Brain MRI is quite abnormal in the disease, but the abnormality is not specific for CADASIL. This is an autosomal dominant disease, meaning that if a person is affected, their children have a 50% chance of having the same disease and other family members are affected. Genetic testing is the easiest and generally most accurate way to make the diagnosis. The disease is steadily progressive with recurrent strokes resulting in significant disability, dementia and in some cases, premature death. There is no specific treatment.

A middle aged man had some transient neurologic abnormalities, migraines and an abnormal MRI of the brain. Genetic testing for CADASIL was sent. The laboratory identified change in Notch 3, the CADASIL gene. The report stated that this was a known disease-associated mutation. The interpretation was confusing to my colleague because the DNA variant should not have led to a change in the protein. (Some amino acids can be coded several ways by the DNA, so a DNA change does not necessary cause a protein change, and without a protein change, disease is quite unlikely.) My colleague called the laboratory director to discuss this unusual situation. The lab director stood by the result and insisted this was CADASIL. Because of the suspicion that this was NOT in fact CADASIL, both of the gentleman's parents were tested (neither of whom had any symptoms relevant to CADASIL) and the mother had the same genetic variant. In her case, the same laboratory reported this as a "known polymorphism", meaning that it was a benign variant not associated with disease.

Ultimately a biopsy was performed to see if the man had other typical findings of CADASIL. None were found. Finally, the same laboratory was sent another sample from the patient. The lab identified the same variant that had been found previously and found in the patient's mother, and this time it was called a known polymorphism. The patient's ultimate diagnosis appears to be multiple sclerosis, treatment for which was delayed by one year due to this error. The bill to the family for all the genetic testing was approximately $10,000. The emotional cost was huge. There was no acknowledgement on the part of the laboratory that there had been an error, despite multiple phone calls regarding this case from the physician involved.

Case 4.
A 33 year old man was seen for clarification of his diagnosis and genetic counseling. He has Charcot Marie Tooth disease, but the type was unknown. He has a young son and wondered if the child could inherit his problems with weakness. His mother and several other relatives were similarly affected. Testing for CMT1A was normal. We then sent testing for CMTX. This is one form of CMT that is inherited in an X-linked fashion (carried on the X-chromosome). If this man has CMTX, then he could not pass it on to a son, since he would only give his son a Y chromosome. If this family has another form of CMT, the risk to his son would be 50%. This was an issue of grave concern for this man as he felt that his life had been significantly impacted by CMT. The CMTX report interpretation read: "This individual possesses a sequence alteration in the coding region of the Cx32 gene which cannot be interpreted as either disease associated or benign polymorphism, and therefore the result is indeterminate". The specific nucleotide change was also listed on the report. By reviewing the nature of the amino acid change, and databases listing the structure of this gene in many lower species, we were able to come to a conclusion that this change is highly likely to be disease causing. We confirmed this be discussion with a research expert in the field and have given appropriate counseling to the patient for CMTX.

Case 4 is one example of a case where the result is "indeterminate". Any time a mutation or alteration in a gene is identified, whether in a research laboratory or a clinical laboratory, the first question to be answered is whether it is simply part of the genetic variability that contributes to making us each an individual, or does it change the function of something essential, leading to disease. There are several approaches that can be taken to try to answer the question. The simplest is to look at the medical literature to see if the change has been reported in other people with the same disease or in the general population. If it is unreported, then one can examine additional information (computer database searches and basic biochemistry), as described in case 3, to make the best possible determination about whether or not the change is disease-related. In a research laboratory, several increasingly complex steps can be taken to clarify the nature of the genetic variation.

Clinicians rely on the genetic testing laboratory director to do the database searches and use their knowledge of biochemistry and physiology to examine the effects of the potential mutation and give the clinician the best possible guidance about whether it is disease-causing or benign. Clinicians generally have neither the time nor the expertise to do that level of analysis. This kind of support is generally viewed as part of the cost of the test (above and beyond the simple technical examination of the DNA). Most genetic testing laboratories in my experience offer this kind of service. If a laboratory fails to provide this service, I generally try to find an alternative laboratory to work with on future patients.

The problem of indeterminate test results is illustrated in Case 4, but I could have presented many more cases. Two similar cases from another institution were recently presented at the Symposium on Neurogenetics at the 2007 Child Neurology Society meeting and were contrasted with reports from a laboratory that provided detailed analysis of genetic variants.

In summary, the lack of choice in laboratories offering genetic testing, as a direct result of the patenting of genes and granting of exclusive contracts, is unusual in medicine and deleterious to patients and practitioners alike. It has led to my limiting my diagnostic testing in some cases, and accepting suboptimal test results in others. It has led to uncounted phone hours attempting to sort out errors and problems, without the simple recourse of choosing a different laboratory. It contributes to unnecessary health care expense. I feel that my ability to provide the best possible care to my patients is compromised by the current situation in genetic testing. Many of my colleagues in clinical genetics and neurology around the country share my concerns.

We are moving into an era when some treatments for genetic diseases will be based, at least in part, on the specific genetic mutation that caused the disease (example: PTC 124 is currently in trials for Duchenne muscular dystrophy and cystic fibrosis patients with point mutations and premature stops). If genetic testing becomes a prerequisite for best therapy, and each of these genetic tests is "owned" by a single, for-profit company without competition, I see no incentive to optimize service and accuracy, or to minimize costs to the patient, resulting in further escalation of health care costs and even greater clinical impact of errors in genetic testing.

Thank you very much for your attention to this issue.

K Mathews

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Mr. BERMAN. I now change your name to Mr. Kushan.

TESTIMONY OF JEFFREY KUSHAN, PARTNER, SIDLEY AUSTIN, LLP, ON BEHALF OF BIOTECHNOLOGY INDUSTRY ORGANZATION (BIO), WASHINGTON, DC

Mr. KUSHAN. Thank you, Mr. Chairman. Thank you, Mr. Chairman.

I am pleased to be here today to provide the views of the Biotechnology Industry Organization on the issue of gene patents. BIO is the principle trade association representing the biotechnology industry. There are more than 1,100 members of BIO. You can find them in every state of the union, and they presently employ more than 1.2 million people in the United States.

Biotechnology is still a young and growing industry. There are about 300 public companies in the biotech industry. At the end of 2005, their market cap was about $410 billion. The remainder of the companies in the biotechnology industry are private companies.

The typical biotech company is a small business with no products, no revenues and running itself on investor funding. Many of these companies are formed to take advantage of a significant scientific discovery or development. These companies focus on performing cutting-edge research aimed at discovering new products and services and bringing them to market. They follow a high-risk, high-reward business model. This model has been a signature of the industry since its inception.

Three fundamental requirements exist for biotech companies that are following this business model: first, scientific innovation; second, adequate funding; and, third, dependable intellectual protection.

I have chosen the word “dependable” in relation to intellectual property intentionally. When a biotech company develops an invention, they must make a judgment on whether the invention can be patented and whether these patent rights can be effectively used when and if they finally get a product to market. That judgment is based on existing legal standards and an assessment.

This certainty in the availability and use of patent rights in the future is critical given the uncertainty that exists on the scientific side of the business and whether they will ever reach the market with a product.

Today’s discussions focus on gene patents. The word “gene patent,” as some of the other panelists have already pointed out, is somewhat imprecise. What is at issue are patents that claim nucleic acids. Nucleic acid inventions are developed following extensive research and development. They rely on sophisticated research on genomic information. The research focuses on deciphering that genetic information and identifying a practical application for using the nucleic acid.

It is important to recognize this is not a debate about the quality of these patents. This is perhaps the one area of the Patent Office that is the most competent, the most high quality of all the areas. The PTF for more than 20 years has been doing extensive research on developing its own first-class examination group. You have more Ph.D.s in the biotech group than any other area, and they certainly know their stuff.

One of my other co-panelists had mentioned that the standards governing patent law in the biotech area have evolved significantly over the last 20 years. I think one thing we can assure you of is that when a patent issues in this sector, it is reflective of a significant advance, the company is deserving of the protection, and that will be used to develop products and bring them to market.

There are three points that I feel need to be addressed today.

First, the biotechnology industry is extremely competitive, and it is a lucrative business. You know, that dynamic is going to create conflicts no matter how you look at it. It is good for companies to have competition. It is also good for companies to be able to develop their own technology, protect it and rely on patents to do so.

You also have to appreciate that the competition is making the industry healthy and strong, and it is also delivering significant benefits for patients as products reach the market. Without that lucrative drive for the incentive for reward on innovation, you will not see the products coming to the market. You will not see the technology reaching the market and form valuable products and services.

It is also a fact that conflicts arise whenever you have a lucrative, competitive market. Patent conflicts also are common in this world, and the biotechnology industry accepts that as part of the equation of doing business in this environment.

Given the dependence on patent rights and the acceptance of the industry that there will be need to resolve disputes over property rights, we are very concerned that there might be some tinkering of the patent system that would alter the equation that so many companies have relied on before they made their investments.

The second point that was raised was the question of using the march-in rights under the Bayh-Dole Act. In the mid-1990's, there was some thought to using that authority in the Bayh-Dole Act to regulate pricing of pharmaceutical products. The only impact we could see from that is that the private companies ran away from the Federal funding because to attach a string like that upstream to invention of a product before you took the funding from the Government basically made that a nonstarter for the companies looking at that source of funding.

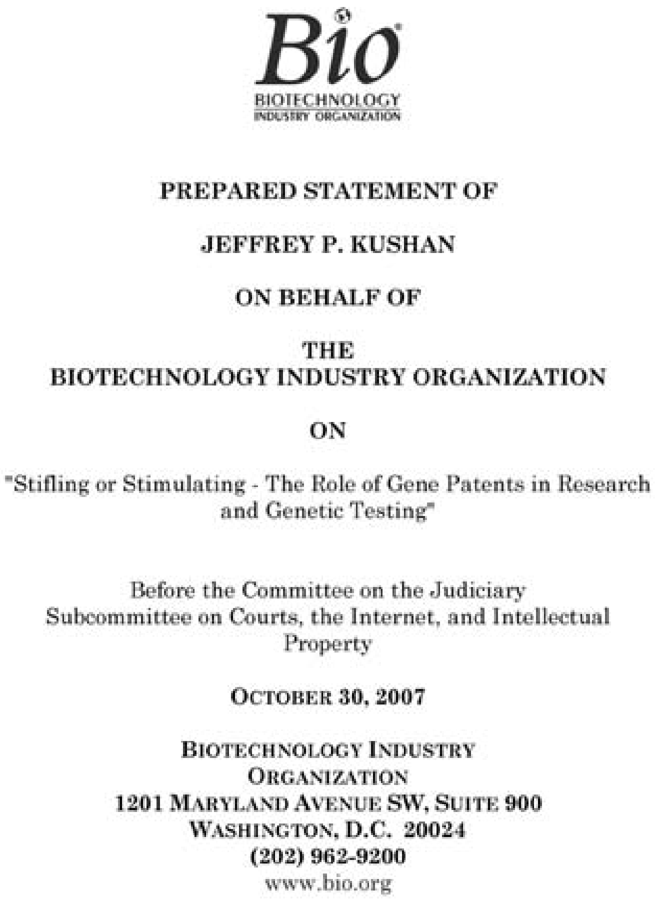
Third is to just touch on the research exemption. I think what we have seen—and Dr. Soderstrom had pointed this out—there are very few instances of patent owners suing universities for many of the reasons he has already pointed out. The *Madey v. Duke* was kind of a weird case involving a particularly unhappy patent owner with an employment dispute with Duke University, and I do not think it is a representative fact pattern that most companies who hold patents see when they are dealing with universities.

So I would just like to conclude in encouraging the Committee to look very carefully at the issue of gene patents and to also carefully consider what impact upstream, downstream that might have if you start to look at changing some of the parameters that companies have relied on before they made their investments in the sector.

Thank you.

[The prepared statement of Mr. Kushan follows:]

PREPARED STATEMENT OF JEFFREY P. KUSHAN



PREPARED STATEMENT OF

JEFFREY P. KUSHAN

ON BEHALF OF

THE
BIOTECHNOLOGY INDUSTRY ORGANIZATION

ON

"Stifling or Stimulating - The Role of Gene Patents in Research and Genetic Testing"

Before the Committee on the Judiciary
Subcommittee on Courts, the Internet, and Intellectual Property

OCTOBER 30, 2007

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Overview

The Biotechnology Industry Organization (BIO) appreciates the opportunity to provide the views of its members on the role of DNA-based inventions in research and innovation. In general, BIO believes that the patent system has proven to be an effective stimulus for developing and bringing to market a wide range of innovations that have delivered innumerable benefits to patients and consumers.

The biotechnology industry today is a thriving, competitive, and dynamic industry. A significant reason for this is the availability of comprehensive and effective patent protection, including for inventions based on nucleic acids. Nucleic acid patents enable start up companies, universities, as well as established companies, to justify the significant investments – whether on the order of millions or hundreds of millions of dollars – that are necessary to discover, develop, bring to market and support products and services based on these nucleic acid inventions.

BIO does not believe issues exist that justify legislation to modify the patent system with regard to nucleic acid inventions. Like any other industry, commercial conflicts can arise regarding use of patented technology. The presence of occasional patent conflicts, or the need to resolve them (including through litigation), does not signal a need for legislative reform. Rather, it is a signal that there is a healthy degree of competition in this sector. And, the benefits delivered by the R&D investments of biotechnology companies far outweighs the incidental costs of resolving these patent disputes.

Background on BIO and the Biotechnology Industry

BIO represents over 1,100 companies, universities and research institutions that use biotechnology to research and develop cutting edge healthcare, agricultural, industrial and environmental products and applications. As of December 31, 2005, there were over 1,400 biotechnology companies established and doing business in the United States, 329 of which were publicly held, having an aggregate market capitalization of over $410 billion. The biotechnology industry has mushroomed since 1992, with U.S. health-care biotech revenues increasing from $8 billion in 1992 to $50.7 billion in 2005. BIO members directly employ more than 1.2 million people, and biotechnology companies can be found in every state of the Union. More than 80 percent of BIO members are small businesses.

The biotechnology industry is one of the most research-intensive industries in the world. In 2005 alone, biotechnology companies spent nearly $20 billion in R&D. Since its inception, the biotechnology industry has raised more than $100 billion in private investment. These investments are paying off. There are more than 400 new drug products and vaccines on the market or in development. These products are now improving, and will continue to improve, the lives of millions of Americans, and offer hope for cures for a wide range of illnesses. Advances in agricultural biotechnology have already had a profound impact on the world's capacity to feed itself, dramatically improving yields of crops while decreasing dependence on chemical pesticides. Industrial biotechnology is affecting numerous sectors of the economy, and is presenting a realistic alternative through biofuel production.

The key to success of the biotechnology industry – across of all its sectors – is a business model that is based on taking significant risks to develop products based on innovation. Specifically, the biotechnology business model is based on making significant investments (often hundreds of millions of dollars) in early stage research and development with the hope that some of these investments and efforts will yield a commercial product. This model has worked despite the fact that it is lengthy (often taking more than a decade) and that most biotechnology R&D investments and efforts do not result in a commercial product reaching the market. It is only by pushing boundaries of science and taking these risks that breakthrough inventions are discovered and converted into commercially viable products and services.

The biotechnology business model requires an environment that, as much as possible, eliminates unpredictability in the commercial sector. One important factor in this environment is the guarantee of patent exclusivity. Specifically, by ensuring that the products or services that may eventually be marketed can be protected from unauthorized copying and use, companies can justify taking risks and making significant R&D investments. Introducing unpredictability by changing the availability of patent rights, or the conditions in which patent rights can be asserted, will adversely affect business environment that is so crucial to supporting innovation in the biotechnology sector.

Patents and the Biotechnology Industry

The biotechnology industry can attribute its current success to two seminal events in 1980; namely, the landmark Supreme Court decision of *Diamond v. Chakrabary*, 447 U.S. 303 (1980), in which the Supreme Court confirmed that key forms of biotechnology inventions including biological materials and living organisms can be patented; and by the passage of the Bayh-Dole Act, which allowed for the efficient transfer of patents on inventions arising from federally-funded research into the private sector.

Patents in the life sciences sector protect the type of products and processes that are integral to companies doing business in the biotech sector. By enabling these companies to prevent the unauthorized use of the patented technology, companies can justify pursuing their research and development efforts. Indeed, it is the guarantee of securing and using rights in the future that companies rely to justify making investments in R&D today.

To illustrate the role of patents in the typical biotechnology venture, consider the following example. A researcher, typically in a university laboratory, discovers a gene which is expressed only by a particular type of cancer cell. This discovery can result in a variety of distinct research and development initiatives – ranging from diagnostic tools for detecting the presence of the gene or its expression product in test samples taken from patients, to therapeutic agents that selectively kill cells that express the gene or inhibit the expression of the gene. As soon as practical after the discovery of the gene and its practical value, patent applications must be filed. Filing the application early ensures that the researcher or its sponsor (a university or startup biotechnology company) can secure rights in the inventions that derive from the discovery, and permits the researcher to publish the results.

The patents based on this early application will be used to justify the investment of millions of dollars into development of these diagnostic and therapeutic agents. Translating this initial discovery into a tangible products can take more than a decade and hundreds of millions of dollars. The exclusivity that patents issued from this early application is what investors will rely upon to provide funding for development of products, and will be a key factor affecting the decision of a larger company to work with the startup company or university that owns the patent to do clinical development of products based on the discovery. Of course, the road to development from this point is long and torturous, has a significant likelihood of failure, and is fraught with other commercial setbacks. However, the faith that the discovery will help improve the lives of patients, and the confidence that patent rights will protect products that are developed, propel the transfer of technology and research and development work that follows.

Patents in the Field of Genomics

The topic of this hearing is "gene patents." Conceptually, this is a misnomer. Patents are not granted on "genes" per se, but on nucleic acid sequences that have a practical application. Genes as they exist in nature cannot be patented. Instead, patents can be secured for discrete nucleic acid sequences that are made after conducting research on genetic information.

Significant advances over the past two decades in research tools, such as the polymerase chain reaction (PCR), gene sequencing technology, and sophisticated computers and analytical tools, coupled with significant public and private investments, have produced a wealth of genomic information and tools for analyzing that information. By performing genomic research, scientists can discover and characterize genes and their functions, and then conduct research to decipher how to exploit the genomic information to produce useful products and services.

Two significant aims of genomic research have been to (i) identify sequences corresponding to proteins that regulate cellular activities, and (ii) to identify "abnormal" sequences and link these sequences to disease states. Once deduced, the "function" or "role" of a gene can provide the basis for developing a practical application of a nucleic acid sequence derived from that gene. This nucleic acid having a practical application – such as whether to enable commercial production of a desired protein the nucleic acid encodes or to provide the basis of a clinical diagnostic tool – is the threshold that must be achieved in order for a nucleic acid to have a practical application, and thus be "useful" in a patent sense. *See, In re Brana*, 51 F.3d 1560 (Fed. Cir. 1992).

A nucleic acid (i.e., a discrete nucleotide sequence), like any other type of chemical compound, is eligible to be patented if it is new, useful, and not obvious. A patent may be granted giving rights in the nucleic acid invention only if it is adequately described in a patent application. This public disclosure is the principle public benefit of the patent system – in exchange for disclosing their invention in a scientifically meaningful way, inventors are awarded a finite period of exclusive rights in the invention that is patented.

Over the patent 20 years, the Congress, the Patent and Trademark Office (PTO) and the courts have been ensuring that this bargain is a good one for the American public. For example, in 1995, Congress changed the term of patents to run 20 years from the date patents are filed, rather than 17 years from the date patents are granted. As a consequence, the fixed period of exclusive rights is now more certain, and in many cases, is shorter, than it had been before 1995. Then, in 1999, the Congress enacted changes to the patent system that require publication of patent applications 18 months after they have been filed. This means that the public gets their part of the bargain – a meaningful public disclosure of the invention – regardless of whether the patent applicant emerges with any rights.

The PTO, almost from the dawn of the biotechnology industry, has been focused on granting high quality patent grants. In 1988, barely years after the first wave of biotechnology applications had been filed, the PTO formed a special new group to focus on examination of biotechnology applications, aggressively devoting resources to accurate examination of biotechnology applications. This group has since grown to more than 485 examiners today, more than 80% of which have advanced degrees, including more than 385 examiners with Ph.D's. This is by far the most technologically advanced and competent group of patent examiners in the PTO today.

A critical threshold for any invention to be patented is that it is new. In the field of biotechnology, this raises two issues. First, to be eligible to be patented, the invention must be claimed in a form that distinguishes it from the form it is found in nature. A nucleic acid patent, thus, cannot be issued with claims that define nucleotide sequences that are indistinguishable from the form in which the nucleic acid exist in nature (e.g., in a human chromosome). A nucleic acid patent, thus, must be limited to a specific nucleotide sequence that does not occur in that form in nature. Second, there is extensive information that has been published regarding genetic sequences. To be patentable, the claim must be distinct from any nucleotide sequence that has been reported in the literature. If the claim covers nucleic acid sequences that are already known from earlier experimental work, the patent should not issue, or if it is, will likely be held invalid.

Other patentability criteria operate to limit the scope of patent rights in the field of nucleic acids. The PTO has aggressively applied these patentability criteria in examining biotechnology applications for more than 25 years. In fact, the PTO has promulgated several sets of guidelines that set forth aggressive examination standards aimed specifically at biotechnology patent applications, such as those claiming nucleic acid inventions.

In 1995, and again in 2001, the PTO issued guidelines relating to the "utility" standard of 35 U.S.C. §101. See, e.g., *Utility Examination Guidelines,* 66 Fed.Reg. 1092 (Jan. 5, 2001). Under these guidelines, the PTO has demanded applicants identify a specific, substantial and credible utility for their inventions. This disclosure must appear in the patent application, which is filed shortly after an invention is made. The guidelines do not permit an applicant to simply guess about what a nucleic acid might be useful for – they require the disclosure to be supported by a scientifically credible basis of support. The PTO has supplemented these guidelines with training materials that illustrate how to apply the standards properly. See, **http://www.uspto.gov/web/offices/pac/dapp/mpep_examguide.html**.

In 2001, the PTO issued guidelines on application of the "written description" requirement of 35 U.S.C. §112, first paragraph. See, *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement*, 66 Fed. Reg. 1099 (2001). As applied by the PTO, the guidelines require applicants to provide a comprehensive written description of what they perceive their invention to be as of the filing date of the patent. The guidelines, in particular, direct examiners to conduct a critical review of whether broad claims, such claims to broad class of related nucleic acids, are adequately supported by the patent disclosure. For example, the guidelines direct examiners to question whether a representative number of nucleic acids covered by a broad "genus" claim are described in the patent application, or whether the applicant has shown that there is a common structural relationship between the sequences and a function shared by all the nucleic acids in the genus. *Id* at 1106. Again, the PTO followed the guidelines with training materials that provide examples of commonly encountered scenarios, with clear guidance on when to impose rejections. See, **http://www.uspto.gov/web/offices/pac/dapp/mpep_examguide.html**.

These PTO efforts have been aided by a series of decisions of the Supreme Court and the Federal Circuit over the past two decades.

As noted above, the principles of broad eligibility for patents on living organisms and materials derived from them has been affirmed by the Supreme Court in *Chakrabarty*, and was again confirmed in 2001 by the Supreme Court in *J.E.M. Ag. Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124 (2001) (holding non-naturally occurring plants eligible to be patented under utility patents).

A series of decisions of the Court of Appeals for the Federal Circuit have both laid the foundation for the PTO guidelines, and affirmed the legitimacy of these guidelines.

- In *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) the Federal Circuit set forth a practical guide for applying the "enablement" requirement of 35 U.S.C. §112, first paragraph. This requirement demands that an applicant provide a disclosure that enables a person skilled in the field of the invention to practice the full scope of the claimed invention. As the court explained, unpredictability in the field of the invention, which is common in the field of biotechnology, often demands a more comprehensive disclosure. The so-called "Wands factors" are a central focus of the PTO examination process in the biotechnology area. See, e.g., MPEP 2164.01(a).
- The principles in the PTO utility guidelines were affirmed by the Federal Circuit in 2005 in the case of *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005). *Fisher* specifically addressed the patentability of expressed sequence tags, which are short nucleic acids produced incidental to the

expression of a gene in a cell. EST sequences correspond to at least part of a gene that encodes a protein, and thus have some value in conducting research to discover a gene or a protein encoded by the gene. The Federal Circuit, largely affirming the rationale of the PTO which had rejected claims under §101 in the case, held that this mere potential for use in discovering a gene was not sufficient to satisfy the specific and substantial utility requirements of §101, which were the focus of the PTO guidelines. In particular, the court observed that labeling the invention as a "research" tool or not was not helpful to the analysis, stating:

> [a]n assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. [The PTO] must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm.

Fisher at 1372. Instead, the court emphasized that the patent applicant must identify in the patent application a utility that (i) is specific to the claimed invention, rather than being generally applicable to all molecules in the class of the invention, and (ii) must be substantial, in that it provides "real world value" (i.e., that "one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public."). The court then held that claims based on the EST sequences described in the application were not sufficient under §101. The Federal Circuit specifically observed that the "...PTO's standards for assessing whether a claimed invention has a specific and substantial utility comport with this court's interpretation of the utility requirement of § 101." *Id.*

- The Federal Circuit has also found the PTO's guidelines concerning the written description requirement to be consistent with the requirements of this section of the patent law. See, Enzo Biochem v. Gen-Probe, 323 F.3d 956, 964 (Fed. Cir. 2002) ("We are persuaded by the Guidelines on this point and adopt the PTO's applicable standard for determining compliance with the written description requirement"); see also, *University of Rochester v. Pharmacia*, 375 F.3d 1303 (Fed. Cir. 2004).

The efforts of the PTO, and the decisions of the Federal Courts, have ensured that patents on nucleic acids that are issued or asserted today are valid, reflect a true inventive contribution, and provide a balanced set of rights for innovators relative to the public at large. In simple terms, given the rigor of examination of patent applications in this sector and the stringent legal standards governing patent eligibility and claim scope, there is no basis for any criticism of the quality of patents issuing that claim nucleic acids or other biotechnology inventions.

Nucleic Acid Patents Are Used In Different Ways by the Biotechnology Industry

Some have identified concerns with "gene patents" and offered solutions that would, as a practical matter, eliminate the possibility of obtaining patents on nucleic acids. Before addressing the merits of those concerns, it is important to appreciate the far-ranging impact such a proposal would have on the biotechnology industry.

Patents on a specified nucleotide sequence give rights to prevent the unauthorized making or use of the nucleotide sequence. This right can be applied in a variety of commercial settings. One use is to incorporate the sequence into a host cell, and use it to produce a protein encoded by that sequence. Another application is to use the sequence to screen samples from patients to detect the presence in the sample of the sequence, which might indicate that the person being tested has a condition that justifies further investigation or treatment. Other uses of the sequence can be envisioned, each having some distinct final outcome (e.g., a product that incorporates the sequence, a product made via use of the sequence, information that provides clinical diagnostic value, a therapy based on interfering with expression of a gene). The same type of patent rights are implicated in each application – patent rights in a discrete nucleotide sequence.

As such, a patent on a nucleic acid has significant commercial value because the single patent can support a variety of distinct commercial applications ranging from producing a new drug product to a new diagnostic agent. Consider the case of a company that has developed a protein that is useful for treating a disorder. This company will use the nucleic acid patent to control which companies, if any, may be authorized to manufacture the protein. If the protein is identical to a protein that occurs in nature, patent rights in the protein may be limited or non-existent. The nucleic acid rights, by contrast, provide practical value by enabling the innovator to control the commercial production of the protein. Without protection for the nucleic acid embodiment of the invention, there may be no exclusivity available that could justify investment in developing the therapeutic product.

Legislation Altering Patent Rights in Nucleic Acid Inventions Would Harm the Biotechnology Industry and Be Inconsistent With WTO Standards

Prohibiting the issuance of patents on nucleic acids would fundamentally disrupt expectations that were set for the industry nearly 30 years ago in *Chakrabarty*. The capacity of a biotechnology company to secure comprehensive commercial protection against free-riding on its investments and efforts has been a crucial factor contributing to the success of the biotechnology industry. Biotechnology companies for nearly three decades have used patents to secure this commercial protection, and count on it in a critical fashion to guide their business development and investment decisions. In a setting where hundreds of millions of dollars of investment must precede the commercial launch of a product, eliminating or even limiting patent protection for a commercially important aspect of the product (i.e., nucleic acids) would be severely disruptive and harm long-settled expectations.

Legislation prohibiting the issuance of nucleic acid patent claims, or limiting use of patents on nucleic acids, also would place the United States out of compliance with its international obligations. For example, under the World Trade Organization Agreement on Trade Related Aspects of Intellectual Property Rights (WTO TRIPS Agreement), WTO members may not exclude protection for specific categories of inventions, such as nucleic acids, or limit their "enjoyment" (i.e., the ability of the owners of those patents to use them). Doing so would run counter to obligations of the United States under Article 27.1, which prohibits discrimination in the availability or enjoyment (i.e., use) of patents and patent rights, based on the field of technology of the invention.

Legislation is Unnecessary

Three different types of concerns have been raised regarding gene patents. None of these concerns merits legislative action, in the view of BIO.

One concern that has been voiced is that the existence of patents on nucleic acids is preventing academic research from being conducted. This perspective is inconsistent with the experiences of BIO and its members. An important historical aspect of the biotechnology industry is its close affiliation with the academic scientific community – particularly professors in universities and in other public research institutions. This relationship is built upon shared principles, such as a desire to advance scientific understanding through both basic and applied research, publication of scientific advances and sharing of information regarding research results.

This concern is based, in part, on fears of an increased frequency of patent infringement assertions by biotechnology companies against universities and other public research institutions following the decision in *Madey v. Duke University*, 307 F.3d 1351 (Fed. Cir. 2002). Most working in this field recognize that unique circumstances were presented by the *Madey* case, in which patent rights in a machine were entangled in a broader dispute between Duke University and an ex-employee. These circumstances are unlikely to be viewed as a harbinger of a new wave of patent litigation by biotechnology companies against universities. And, since 2002, there has not been a significant increase in patent infringement actions against university researchers. Certainly, if a university researcher is being supported by a commercial competitor of a patent owner to develop a competing product that infringes a patent, that researcher may become part of a broader landscape of commercial disputes between the companies. But, concerns that basic research will face significant new obstacles from patent litigation patent are unfounded and not borne out by experience, either from before or after the *Madey* decision.

A similar theoretical concern has been expressed that the number of patents issued in the field of biotechnology will create an overall impediment to the performance of research or in the development of products. The so-called "anticommons" effect, as hypothesized by Drs. Heller and Eisenberg, *Science*, vol. 280, (May 1998), was that the "overpatenting" of biotechnology inventions would stifle research and development in the biotechnology sector. Nearly a decade later, the conflicts hypothesized about in the paper have not materialized. Instead, research and development activities, both in the public and private sectors, has continued to enjoy vigorous growth. A summary of the paper and experiences since it was published is provided as Attachment C to this testimony.

Another concern that has been voiced is that gene patents are impeding the delivery of clinical diagnostic services. Examples have been identified of disputes between companies that own patents on nucleic acids and entities attempting to perform clinical testing for gene-linked diseases. The fact that only one or two disputes of this type have been identified despite the fact that thousands of patents have been issued relating to nucleic acids, in one sense, confirms that the vast majority of gene patents do not create significant impediments to performing clinical diagnostic testing.

Finally, concerns have been expressed that patent rights in nucleic acids will confer rights to control use of genetic information, including by individuals. Patents give rights only in the making, using, selling, offering for sale or importation into the United States of what is patented. In the case of a patent on a nucleic acid, this means that the patent can be used vis-à-vis entities that make or use the nucleic acid that has been patented. Dissemination and use of information about the nucleic acid is part of the bargain of the patent system -- patent rights in a nucleic acid cannot be used to stop use of the dissemination or use of information *per se*.

The granting of valid patent rights, in response to investments and innovative activity, gives the innovator a certain degree of discretion to pursue and exploit the patent rights. To the extent that the business model pursued by a company is impractical, the market should and will respond to address the shortcomings of that business model. It should also be kept in mind that patent rights are inherently limited; they give the owner of the patent the right to prevent others from using the patented invention without authorization. Patents do not convey positive rights to perform diagnostic testing, impose impractical or unlawful conditions (through contract or otherwise), or to waive compliance with laws governing competition or the regulation of human diagnostic products. Patents only provide the right to prevent others from using the patented invention.

From a broader perspective, BIO submits that granting patents in exchange for public disclosure of inventions – including for nucleic acid inventions that are new, useful, non-obvious and adequately disclosed – reflects sound public policy. The benefits after nearly 30 years of experience cannot be contested – more than a thousand companies, employing more than a million highly skilled people, and producing hundreds of life-saving and life-changing products and services. Indeed, the biotechnology industry is proof that the patent system is working as it should – promoting billions of dollars of investments in crucially important research and development, generating millions of jobs, and delivering new hope to patients and consumers.

Conclusion

The U.S. patent system allows for broad subject matter eligibility. This system has served this country well over the past thirty years. Everyday, new innovative products enter the market place, and every day, a new discovery is made in biotechnology. The House Subcommittee is to be commended for undertaking this examination of the role of gene, nucleic acid based system. In BIO's view, altering the legal standards of eligibility for gene based inventions, or limiting the ability of innovators to use gene patents, would seriously harm the biotechnology industry. BIO appreciates the opportunity to provide insight into the role of gene based patents in the growth of the biotech industry and to describe the nature of the industry and its contributions to the improvement of the human condition.

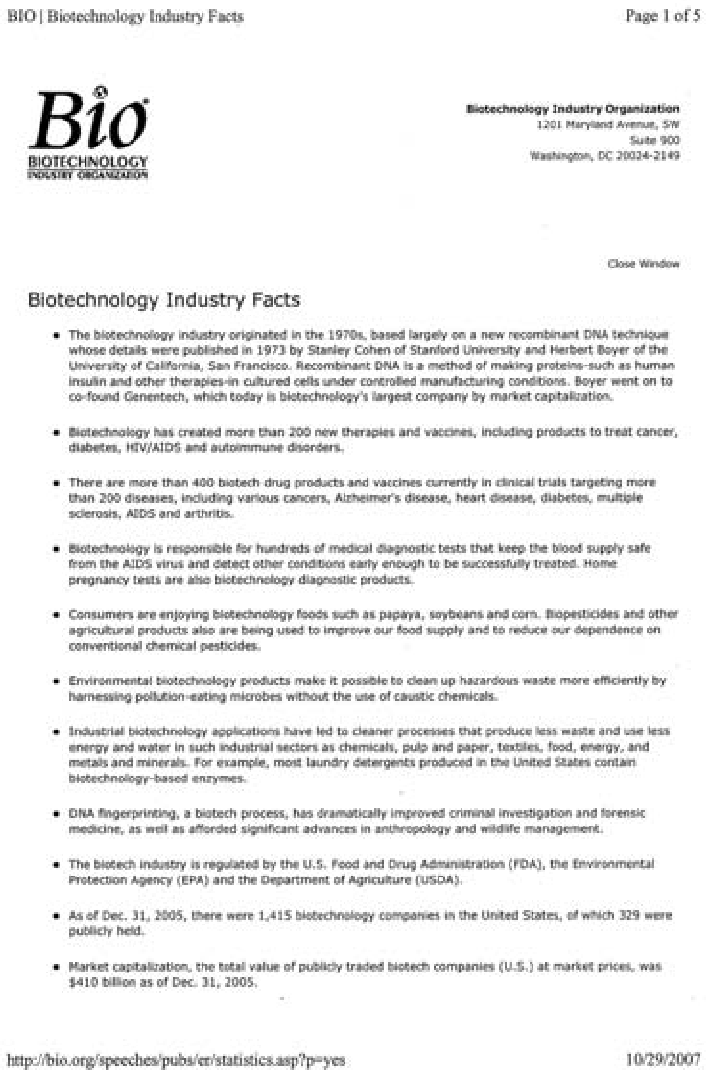
Attachments

A. Biotechnology Industry Facts

B. Ted Buckley, *The Myth of the Anticommons* (May 31, 2007)

C. BIO Position on Research use Exemption

D. BIO FAQ on Gene Patents



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Biotechnology Industry Facts

- The biotechnology industry originated in the 1970s, based largely on a new recombinant DNA technique whose details were published in 1973 by Stanley Cohen of Stanford University and Herbert Boyer of the University of California, San Francisco. Recombinant DNA is a method of making proteins-such as human insulin and other therapies-in cultured cells under controlled manufacturing conditions. Boyer went on to co-found Genentech, which today is biotechnology's largest company by market capitalization.

- Biotechnology has created more than 200 new therapies and vaccines, including products to treat cancer, diabetes, HIV/AIDS and autoimmune disorders.

- There are more than 400 biotech drug products and vaccines currently in clinical trials targeting more than 200 diseases, including various cancers, Alzheimer's disease, heart disease, diabetes, multiple sclerosis, AIDS and arthritis.

- Biotechnology is responsible for hundreds of medical diagnostic tests that keep the blood supply safe from the AIDS virus and detect other conditions early enough to be successfully treated. Home pregnancy tests are also biotechnology diagnostic products.

- Consumers are enjoying biotechnology foods such as papaya, soybeans and corn. Biopesticides and other agricultural products also are being used to improve our food supply and to reduce our dependence on conventional chemical pesticides.

- Environmental biotechnology products make it possible to clean up hazardous waste more efficiently by harnessing pollution-eating microbes without the use of caustic chemicals.

- Industrial biotechnology applications have led to cleaner processes that produce less waste and use less energy and water in such industrial sectors as chemicals, pulp and paper, textiles, food, energy, and metals and minerals. For example, most laundry detergents produced in the United States contain biotechnology-based enzymes.

- DNA fingerprinting, a biotech process, has dramatically improved criminal investigation and forensic medicine, as well as afforded significant advances in anthropology and wildlife management.

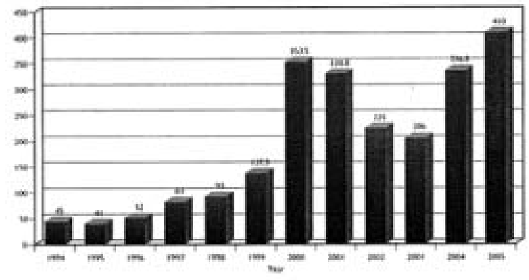
- The biotech industry is regulated by the U.S. Food and Drug Administration (FDA), the Environmental Protection Agency (EPA) and the Department of Agriculture (USDA).

- As of Dec. 31, 2005, there were 1,415 biotechnology companies in the United States, of which 329 were publicly held.

- Market capitalization, the total value of publicly traded biotech companies (U.S.) at market prices, was $410 billion as of Dec. 31, 2005.

- The biotechnology industry has mushroomed since 1992, with U.S. health-care biotech revenues increasing from $8 billion in 1992 to $50.7 billion in 2005.
- Biotechnology is one of the most research-intensive industries in the world. The U.S. biotech industry spent $19.8 billion on research and development in 2005.
- The top five biotech companies invested an average of $130,000 per employee in R&D in 2005.
- In 1982, recombinant human insulin became the first biotech therapy to earn FDA approval. The product was developed by Genentech and Eli Lilly and Co.
- Corporate partnering has been critical to biotech success. In 2005, biotech companies signed 564 new agreements with pharmaceutical firms and 354 with fellow biotechs, according to BioWorld.
- Most biotechnology companies are young companies developing their first products and depend on investor capital for survival. Biotechnology attracted more than $20 billion in financing in 2005 and has raised more than $100 billion since 2000.
- The biosciences-including not just biotechnology but all life sciences activities-employed 1.2 million people in the United States in 2004 and generated an additional 5.8 million related jobs.
- The average annual wage of U.S. bioscience workers was $65,775 in 2004, more than $26,000 greater than the average private sector annual wage.
- Bioethanol-made from crop wastes using biotech enzymes-could meet a quarter of U.S. energy needs by 2025.
- The Biotechnology Industry Organization (BIO) was founded in 1993 to represent biotechnology companies at the local, state, federal and international levels. As of December 2006, BIO's membership consisted of more than 1,100 biotechnology companies, academic centers, state and local associations and related enterprises.

Market Capitalization, 1994-2005*



* Amounts are in U.S. dollars in billions
Sources:

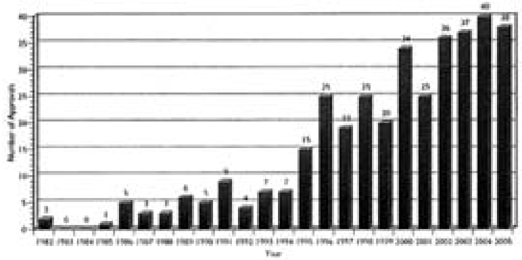
Ernst & Young LLP
BioWorld

U.S. Biotech Industry Statistics: 1994-2005*

Year	2005	2004	2003	2002	2001	2000	1999	1998	1997	1996	1995	1994
Sales	32.1	28.1	28.4	24.3	21.4	19.3	16.1	14.5	13	10.8	9.3	7.7
Revenues	50.7	43.8	39.2	29.6	29.6	26.7	22.3	20.2	17.4	14.6	12.7	11.2
R&D Expense	19.8	19.6	17.9	20.5	15.7	14.2	10.7	10.6	9.0	7.9	7.7	7.0
Net Loss	4.1	6.8	5.4	9.4	4.6	5.6	4.4	4.1	4.5	4.6	4.1	3.6
No. of Public Companies	329	331	314	318	342	339	300	316	317	294	260	265
No. of Companies	1,415	1,346	1,473	1,466	1,457	1,379	1,273	1,311	1,274	1,287	1,308	1,311

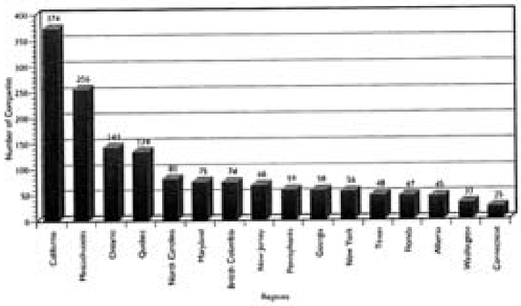
*Amounts are U.S. dollars in billions.
Source:
Ernst & Young LLP, annual biotechnology industry reports, 1995–2006. Financial data based primarily on fiscal-year financial statements of publicly traded companies.

New Biotech Drug and Vaccine Approvals/ New Indication Approvals by Year



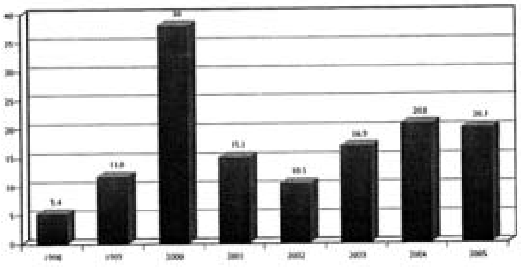
Source:
BIO

North American Biotech Companies by State and Province



Source:
Ernst & Young LLP

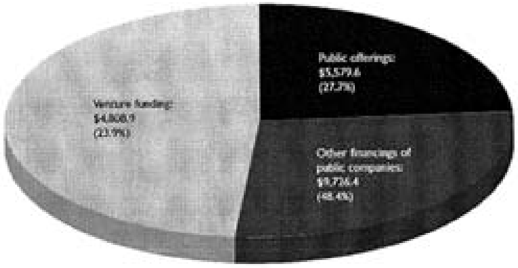
Total Financing, 1998-2005 (in billions of U.S. dollars)



Source:
BioWorld

Biotech Industry Financing, 2005

Total: $20,114.9 Million
(all figures in millions)



Source:
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The Myth of the Anticommons

Ted Buckley, Ph.D.
BIO Director of Economic Policy
May 31, 2007

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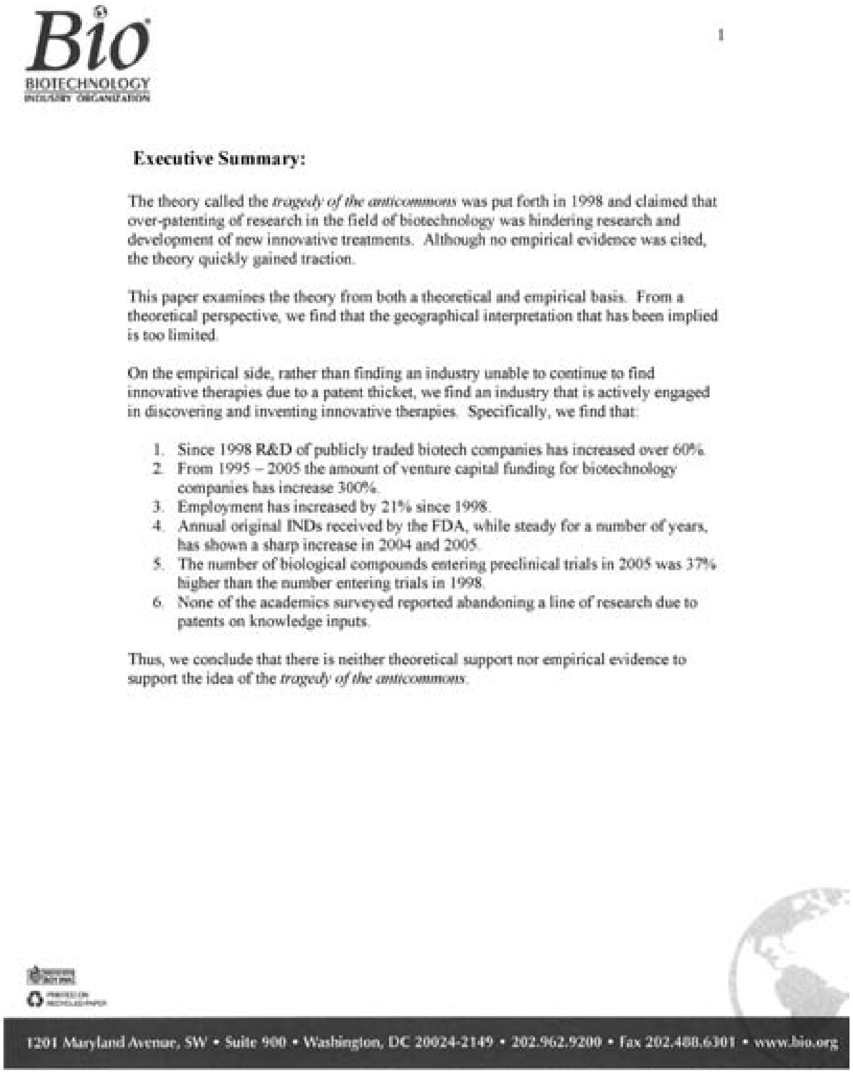


BIOTECHNOLOGY INDUSTRY ORGANIZATION

Executive Summary:

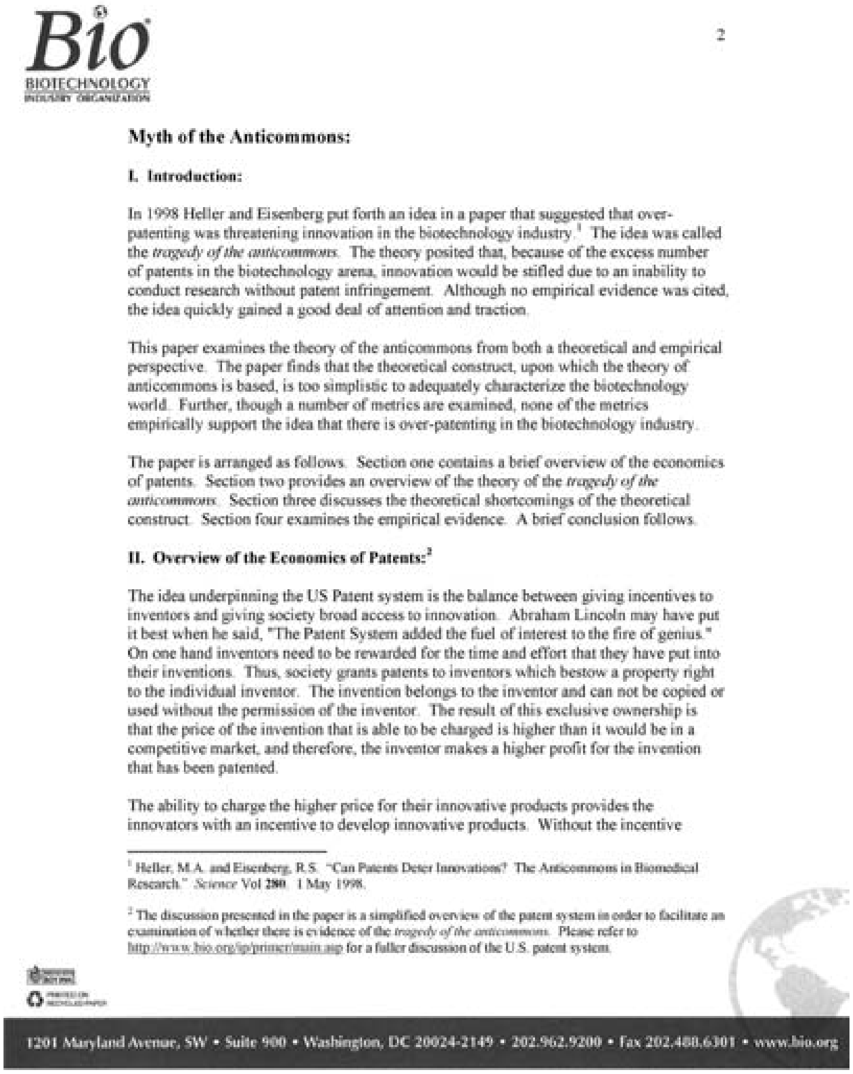
The theory called the *tragedy of the anticommons* was put forth in 1998 and claimed that over-patenting of research in the field of biotechnology was hindering research and development of new innovative treatments. Although no empirical evidence was cited, the theory quickly gained traction.

This paper examines the theory from both a theoretical and empirical basis. From a theoretical perspective, we find that the geographical interpretation that has been implied is too limited.

On the empirical side, rather than finding an industry unable to continue to find innovative therapies due to a patent thicket, we find an industry that is actively engaged in discovering and inventing innovative therapies. Specifically, we find that:

1. Since 1998 R&D of publicly traded biotech companies has increased over 60%.
2. From 1995 – 2005 the amount of venture capital funding for biotechnology companies has increase 300%.
3. Employment has increased by 21% since 1998.
4. Annual original INDs received by the FDA, while steady for a number of years, has shown a sharp increase in 2004 and 2005.
5. The number of biological compounds entering preclinical trials in 2005 was 37% higher than the number entering trials in 1998.
6. None of the academics surveyed reported abandoning a line of research due to patents on knowledge inputs.

Thus, we conclude that there is neither theoretical support nor empirical evidence to support the idea of the *tragedy of the anticommons*.



Myth of the Anticommons:

I. Introduction:

In 1998 Heller and Eisenberg put forth an idea in a paper that suggested that over-patenting was threatening innovation in the biotechnology industry.[1] The idea was called the *tragedy of the anticommons*. The theory posited that, because of the excess number of patents in the biotechnology arena, innovation would be stifled due to an inability to conduct research without patent infringement. Although no empirical evidence was cited, the idea quickly gained a good deal of attention and traction.

This paper examines the theory of the anticommons from both a theoretical and empirical perspective. The paper finds that the theoretical construct, upon which the theory of anticommons is based, is too simplistic to adequately characterize the biotechnology world. Further, though a number of metrics are examined, none of the metrics empirically support the idea that there is over-patenting in the biotechnology industry.

The paper is arranged as follows. Section one contains a brief overview of the economics of patents. Section two provides an overview of the theory of the *tragedy of the anticommons*. Section three discusses the theoretical shortcomings of the theoretical construct. Section four examines the empirical evidence. A brief conclusion follows.

II. Overview of the Economics of Patents:[2]

The idea underpinning the US Patent system is the balance between giving incentives to inventors and giving society broad access to innovation. Abraham Lincoln may have put it best when he said, "The Patent System added the fuel of interest to the fire of genius." On one hand inventors need to be rewarded for the time and effort that they have put into their inventions. Thus, society grants patents to inventors which bestow a property right to the individual inventor. The invention belongs to the inventor and can not be copied or used without the permission of the inventor. The result of this exclusive ownership is that the price of the invention that is able to be charged is higher than it would be in a competitive market, and therefore, the inventor makes a higher profit for the invention that has been patented.

The ability to charge the higher price for their innovative products provides the innovators with an incentive to develop innovative products. Without the incentive provided by the patent, the pace of innovation would slow because inventors would not be rewarded as much for the time, effort and risk that it took to develop the innovation. Indeed, intellectual property protection has been found to be a significant determinant of economic growth.[3]

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[1] Heller, M.A. and Eisenberg, R.S. "Can Patents Deter Innovations? The Anticommons in Biomedical Research." *Science* Vol **280**. 1 May 1998.

[2] The discussion presented in the paper is a simplified overview of the patent system in order to facilitate an examination of whether there is evidence of the *tragedy of the anticommons*. Please refer to http://www.bio.org/ip/primer/main.asp for a fuller discussion of the U.S. patent system.

The patent system is especially important to the biotechnology industry.[4] Each biopharmaceutical that is brought to market requires on average $1.2 billion in research and development. The cost is high for a number of reasons. The reasons include the number of failures that occur along the way. For every biopharmaceutical that is brought to market, there are approximately10,000 failed attempts. In addition, the time to go through clinical development and regulatory approval to market for the biopharmaceutical is 97.7 months on average.[5,6] Finally, the cost of the clinical trials is quite high and has risen substantially in the past decade. On average the cost of research and development rose 7.5% above the annual rate of inflation during the 1990s, the latest years for which figures are available.[7] Patents granted on a biotechnological innovation allow the inventors to recoup the research and development costs which have been invested.

III. Overview of the Anticommons Argument:

As has been discussed, patents are central to the development of innovative therapies in the biotechnology industry. However, in 1998 an idea was put forth that suggested that patents, instead of encouraging innovation, had the potential to actually stifle innovation in the biotechnology industry. This stifling of innovation was called the *tragedy of the anticommons*.[8] The authors posit that innovation may be stifled if there are too many owners who may exclude others from a scarce resource. Specifically, if there are too many patent holders of upstream technology, they may inhibit downstream innovation because of transaction costs and strategic behaviors. Imagine that a biotechnology company seeks to do research in a particular area to bring an innovative therapy to market and that in order to do research in this area the company must use a set of knowledge inputs. Further, suppose that each of the knowledge inputs has been patented by a different company. In order for the biotechnology company to proceed with the research, it must first receive permission from each of the patent holders to use the patent holder's knowledge input for its research.

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[3] Gould, D. M. and Gruben W. C. "The role of intellectual property rights in economic growth." *Journal of Development Economics* Vol **48** (1996) 323 – 350.

[4] See for example, Cohen, W. M., Nelson R. R. and Walsh, J. P. "Protecting their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (Or Not)." NBER Working Paper 7552. February 2000.

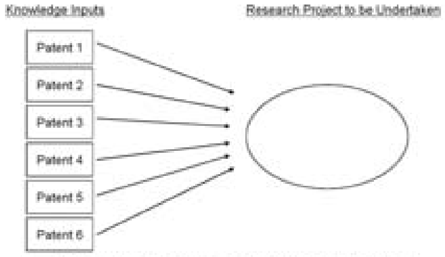
[5] DiMasi, Joseph A. and Henry G. Grabowski. "The Cost of Biopharmaceutical R&D: Is Biotech Different?" *Managerial and Decision Economics*. Forthcoming.

[6] Note: This does not include pre-clinical time of development.

[7] DiMasi, J. A., Hansen, R. W. and Grabowski, H. G. "The price of innovation: new estimates of drug development costs." *Journal of Health Economics* 22 (2003).

[8] Heller, M. A. and Eisenberg, R. S. "Can Patents Deter Innovations? The Anticommons in Biomedical Research." *Science* Vol **280**. 1 May 1998.

Figure 1:



In this case the company would need to obtain permission from 6 different parties before it could undertake the research project

Getting permission may take considerable time and may require considerable money. Thus, the research to bring an innovative therapy to market may be delayed, may cost more or may not take place if the company can not obtain permission from all of the upstream patent holders. In this scenario one patent holder in the set of knowledge inputs could suppress the research by not granting permission for the biotechnology company to use its patented input.

IV. Theoretical Shortcomings of the Anticommons:

The theory outlined above is appealing for its simple elegance. However, the simplicity of the argument is one of its short comings. An implicit part of the argument is that there is a scarcity to the biological commons akin to a geographical scarcity. Indeed, in responding to Heller's and Einsberg's call for a formal economic model to be developed, Buchanan and Yoon developed an economic model and illustrated it geometrically.[9] Further, in another paper that discusses the *tragedy of the anticommons* Scherer states, "The problem is analogous to conditions on the Rhine River during the 18th Century. Over the 85-kilometer stretch between Mainz and Koblenz in 1780, there were nine toll stations…"[10] The result of the excessive number of tolls was a significantly lower amount of traffic on the river.

The geographic analogy is appealing but is flawed when applied to the biotechnology industry. In the examples above, there is a single starting point and a single ending point. In addition in the Rhine River analogy there is only one route from the starting point to the ending point. However, the "geography" in the biopharmaceutical world is much more complex than geography that is described in the world of the anticommons. In biotechnology world there are many starting points and many routes that will lead to the desired ending point, which in this case is an innovative therapy. In applying the "geography" of the biopharmaceutical world to the Rhine River analogy, imagine that a shipper wants to transport good from Mainz to Koblenz but is faced with having to go through nine toll stations on the river. Whereas in the 18th century, the shipper had no other option but to traverse the river, in the 21st century biotechnology world, the shipper has alternative routes, such as roads, rail or air. Thus, the shipper can reach the desired ending point by going around the river tolls.[11]

The idea of going around a toll is well known in the biopharmaceutical industry, as well as other industries, and is called inventing around a patent. An illustrative example is the class of pharmaceuticals called statins, which are medicines designed to lower blood cholesterol levels. In this case, the desired endpoint is a lower blood cholesterol level. According to the geographical example above, there is only one route to the desired endpoint and thus, one would expect only one statin to be on the market. However, there are more than five statin products on the market presently. The statins are but one class among many therapeutic classes of pharmaceuticals in which there are two or more products. There are multiple products in clinical testing for the treatment of breast cancer that utilize a variety of mechanisms of action. Some of these products' mechanisms of action overlap with the mechanisms of action utilized by other products.[12] Likewise, there are multiple products being developed for the treatment of chronic myeloid

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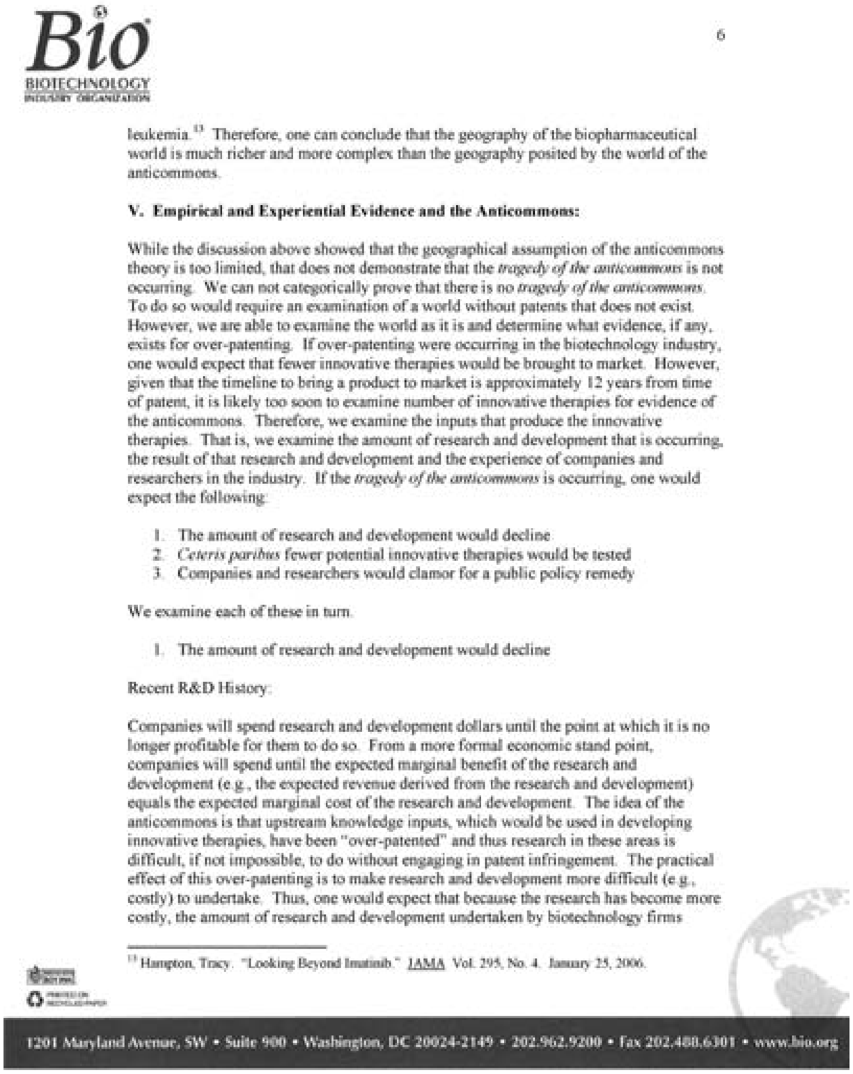
[9] Buchanan, J. M. and Yoon, Y. J. "Symmetric Tragedies: Commons and Anticommons." *Journal of Law and Economics* Vol. **43**, No. **1**. (April 2000).

[10] Scherer, F. M. "The Economics of Human Gene Patents." *Academic Medicine* Vol. 77, No. **12** (December 2002) Part 2, p. 1363.

[11] Epstein, R. A. and Kuhlik, B. N. "Is there a Biomedical Anticommons?" *Regulation* Summer 2004.

[12] Waltz, Emily. "GlaxoSmithKline Cancer Drug Threatens Herceptin Market." Nature Biotechnology Vol. 23, No. 12. December 2005.



leukemia.[13] Therefore, one can conclude that the geography of the biopharmaceutical world is much richer and more complex than the geography posited by the world of the anticommons.

V. Empirical and Experiential Evidence and the Anticommons:

While the discussion above showed that the geographical assumption of the anticommons theory is too limited, that does not demonstrate that the *tragedy of the anticommons* is not occurring. We can not categorically prove that there is no *tragedy of the anticommons*. To do so would require an examination of a world without patents that does not exist. However, we are able to examine the world as it is and determine what evidence, if any, exists for over-patenting. If over-patenting were occurring in the biotechnology industry, one would expect that fewer innovative therapies would be brought to market. However, given that the timeline to bring a product to market is approximately 12 years from time of patent, it is likely too soon to examine number of innovative therapies for evidence of the anticommons. Therefore, we examine the inputs that produce the innovative therapies. That is, we examine the amount of research and development that is occurring, the result of that research and development and the experience of companies and researchers in the industry. If the *tragedy of the anticommons* is occurring, one would expect the following:

1. The amount of research and development would decline
2. *Ceteris paribus* fewer potential innovative therapies would be tested
3. Companies and researchers would clamor for a public policy remedy

We examine each of these in turn.

1. The amount of research and development would decline

Recent R&D History:

Companies will spend research and development dollars until the point at which it is no longer profitable for them to do so. From a more formal economic stand point, companies will spend until the expected marginal benefit of the research and development (e.g., the expected revenue derived from the research and development) equals the expected marginal cost of the research and development. The idea of the anticommons is that upstream knowledge inputs, which would be used in developing innovative therapies, have been "over-patented" and thus research in these areas is difficult, if not impossible, to do without engaging in patent infringement. The practical effect of this over-patenting is to make research and development more difficult (e.g., costly) to undertake. Thus, one would expect that because the research has become more costly, the amount of research and development undertaken by biotechnology firms would decrease. However, if one examines the amount spent on biotechnology research and development, the evidence does not indicate that *tragedy of the anticommons* is occurring.

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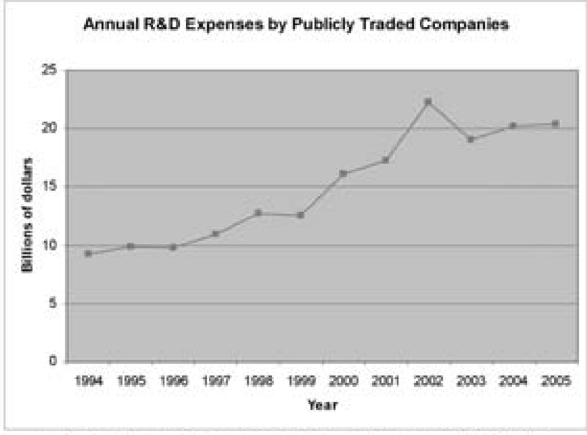
[13] Hampton, Tracy. "Looking Beyond Imatinib." JAMA. Vol. 295, No. 4. January 25, 2006.

Figure 2:



Sources: Ernst & Young LLP, annual biotechnology industry reports, 1993–2006. Financial data based primarily on fiscal-year financial statements of publicly traded companies; constant 2005 dollars.

Figure 2 indicates that the amount of research and development by publicly traded companies in the biotechnology arena has grown substantially over the past decade. Indeed, since 1998 when the *tragedy of the anticommons* was posited, R&D has increased by over 60%.[14]

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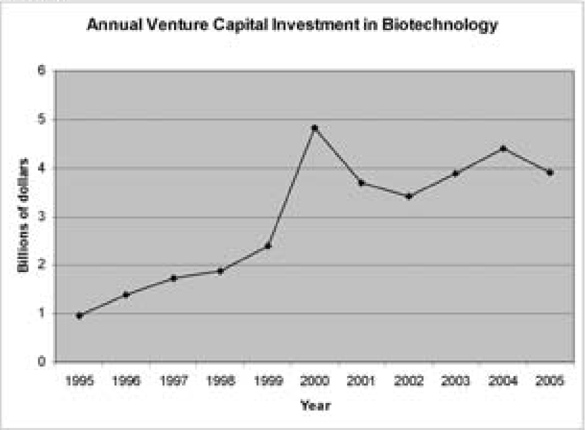
[14] However, one could argue that perhaps the cost of doing research and development has actually decreased during the time period. If the costs decreased at a faster rate than the cost increase associated with the *tragedy of the anticommons*, one could argue that the investment in research and development would therefore increase. However, according to DiMasi, the cost of research and development of innovative therapies has increased at a rate of 7.5% over and above the cost of inflation during the 1990s. DiMasi J. A., Hansen, R. W. and Grabowski H. G. "The price of innovation: new estimates of drug development costs." *Journal of Health Economics* 22 (2003).

While figure 1 focuses on publicly traded companies, privately held biotechnology companies play a pivotal role in the biotechnology industry.[15] Much of the funding for these companies comes from the venture capital (VC) community. If companies were unable to perform research and development due to the presence of the anticommons, one would expect the VC investment in biotechnology to dry up.

Figure 3:



Source: National Venture Capital Association; constant 2005 dollars

Figure 3 shows that the amount of VC has increased substantially in the past decade. In 2005 the amount of VC funding was almost $4 billion, up 300% from 1995.

Another aspect of research is the number of personnel. If the industry were experiencing a significant slow down due to the *tragedy of the anticommons* and the inability to pursue research on innovative therapies, one would expect that the difficulties of the industry would be reflected in a decrease in the number of industry employees. However, biotechnology employment has risen over the past decade.

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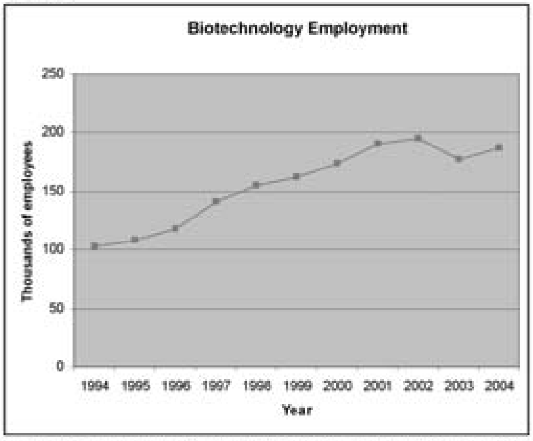
[15] Indeed, according to figures in Ernst and Young's Beyond Borders 2006 three quarters of the U.S. biotechnology companies in 2005 were privately held.

Figure 4:



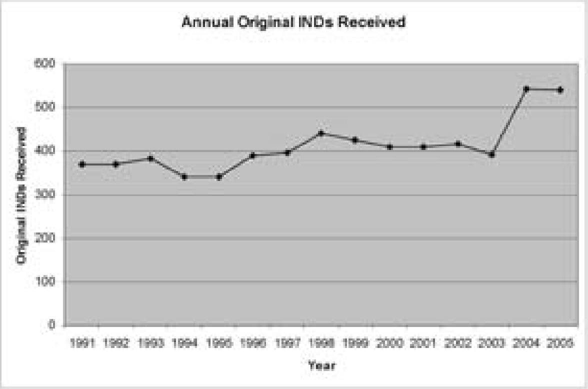
Sources: Ernst & Young LLP, annual biotechnology industry reports, 1993–2005.

Since 1998, the number of employees has increased by 21%. Thus, instead of seeing what one would expect if an industry were experiencing the *tragedy of the anticommons* – lower research and development and with it falling employment – one observes an industry which is increasing research and development levels and increasing employment.

2. *Ceteris paribus* fewer potential innovative therapies would be tested

If the *tragedy of the anticommons* were occurring one would expect that the R&D that was being undertaken would be less efficient. That is, because so many of the knowledge inputs had patents that needed to be licensed or invented around, the research projects would take longer or the research projects would be abandoned altogether. As a result of the increased difficulty of doing research, the number of innovative therapies would decrease. However, given the long lead time that it takes to research and develop an innovative therapy and bring it to market, approximately 12 years, it may be too early to see evidence of the *tragedy of the anticommons*. Therefore, we examine the number of annual Investigational New Drug (IND) submissions, which would be affected in a similar way. Because of the shorter timeframe, if the *tragedy of the anticommons* were occurring, one would expect the number to have decreased.[16]

Figure 5:



Source: FDA, Parexel's Bio/Pharmaceutical R&D Statistical Sourcebook 2006/2007

One would expect the number of INDs to drop if the *tragedy of the anticommons* were occurring. One finds a relatively stable number of INDs being originated annually from 1991 – 1998, the seven year time period before the *tragedy of the anticommons* was posited, and a relatively stable number of INDs being originated from 1998 – 2003. However, there is a sharp increase in the number of original INDs received in 2004 and 2005. These years are precisely the time period when one would expect a decrease if over-patenting were starting to occur in 1998. One would expect a decrease in INDs approximately six to seven years after the phenomenon began to occur because pre-clinical testing (that is the time from a drug being patented until it reaches the IND stage) takes on average between 3 – 6 years. If there were an anticommons problem, it would take 3 – 6 years to manifest.

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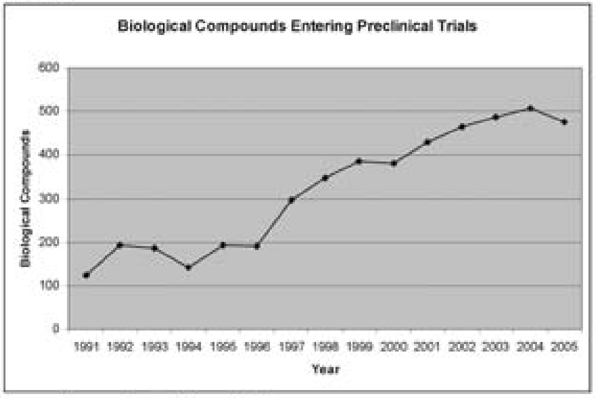
[16] Because biotechnological inputs are used for the development of both small molecule therapies and therapeutic biologics, we examine both in turn.

Next, we examine the number of biological compounds that enter preclinical testing on an annual basis.

Figure 6:



Source: Pharmaprojects, Informa Healthcare

Rather than finding a decrease in the number of biological compounds entering preclinical trials, we find there has been a substantial increase in the number of biological compounds entering preclinical trials both before and after 1998. While the percentage growth has dropped from the 1991 – 1998 to the 1998 – 2005 time periods, in 2005 there were still more than 37% more compounds entering preclinical trials every year than were entering in 1998. This finding is inconsistent with research being stifled or hampered as one would expect to find if the *tragedy of the anticommons* were occurring.

3. Companies and researchers would clamor for a public policy remedy

A substantial number of members of the Biotechnology Industry Organization (BIO), the trade association for the biotechnology industry, are companies who depend on the ability to research and develop innovative therapies. Thus, if there were a *tragedy of the anticommons*, one would expect that BIO would be clamoring for a public policy remedy especially patent reform. However, rather than implying that there is a *tragedy of the anticommons* which is impeding research, BIO's position implies that the patent system encourages innovation. That is, the patent system is not hindering innovation, but rather, the patent system is allowing companies to engage in research and development of innovative therapies.[17]

The *tragedy of the anticommons* focuses specifically on the patenting of upstream research. However, BIO's position specifically supports the patenting of "novel and useful nucleotide sequences..." BIO also supports patenting research tools which, like nucleotide sequences, are akin to the knowledge inputs that the *tragedy of the anticommons* discusses. Further, BIO's position fundamentally opposes the notion that patents on this broad array of biotechnology inventions are hindering innovation. BIO says unequivocally that it supports patenting of these types of inventions. In addition, it affirms that intellectual property rights are a prerequisite for the commercial success of these companies and for future innovation in these knowledge inputs.

While the discussion above focuses on companies and shows no evidence of the anticommons, one may argue that perhaps the *tragedy of the anticommons* is affecting academic researchers rather than companies. The National Academy of Sciences commissioned a study to examine the issue.[18] Walsh *et al* surveyed 414 academic researchers from universities, non-profits and government labs to examine whether their research had been impacted by patents. The authors found that only 1% of the academic respondents stated that they had experienced delays on their projects of more than a month due to patents on knowledge inputs. None of the academics reported abandoning a line of research due to patents on knowledge inputs.

Thus, neither biotechnology companies nor academic researchers are claiming to be adversely affecting by the patenting that is occurring in the biotechnology arena. Indeed, none of the academic researchers surveyed have abandoned research because of patent issues. Further, biotechnology companies have stated not only are patents not hurting them, but on the contrary the ability to patent is a prerequisite for commercial success.

We find no evidence of a *tragedy of the anticommons* either among companies or among the researchers who work in academic, non-profit or governmental settings.

VI. Conclusion:

The *tragedy of the anticommons* is an elegant and compelling theory. The theory claims, that instead of encouraging innovation as patents have been found to do in the biopharmaceutical industry, the patenting that has been occurring in the 1990s has the potential to hinder innovation. However, as has been discussed, the theoretical construct of the anticommons world is too simplistic to describe the world of biotechnology. We acknowledge that we can not categorically state that there is no *tragedy of the anticommons*. To do so would require an examination of a world without patents that does not exist. However, we are able to examine the world as it is and determine what evidence there exists for over-patenting. Indeed, if over-patenting were occurring, the outcome of this over-patenting would be "fewer useful products for improving human health."[19] Because of the long development time of innovative therapeutic products, we inspect the inputs of those products. The first input is R&D. If there were a *tragedy of the anticommons*, one would expect that the amount of R&D would decline because of the increased difficulty of undertaking research. Yet, we find the exact opposite. R&D in both the publicly traded and privately held biotechnology companies is increasing. Further, we find that the number of people employed in the industry is increasing over time. Next, we inspect the pipelines of biopharmaceutical industry. If the research were becoming more difficult, one would expect that the number of innovative therapies in testing would be decreasing. Rather, we find the opposite. We find that the pipeline of both chemically and biologically based innovative therapies is expanding. Thus, the information that we examine paints a picture of an industry that is growing in terms of research and development with an increasing number of products in the pipeline. The argument could be made that perhaps researchers – either those in industry or in academia - are encountering problems that are not reflected in the R&D figures or in the numbers associated with the product development pipeline. However, the biotechnology industry is strongly supportive of the patent system and contends that it encourages innovation. Thus, industry is not supportive of the idea that over-patenting is occurring and hindering its ability to bring innovative therapies to the marketplace. Further, none of the academic researchers surveyed by Walsh *et al* abandoned their line of research due to patents on knowledge inputs. Therefore, we conclude, based on both empirical and experiential evidence, that there is no support for the idea that a *tragedy of the anticommons* is occurring in the biotechnology industry.

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[17] BIO's Principles for Patent Reform Approved March 29, 2004 Board IP Standing Committee.

[18] Walsh, J. P., Cho, C. and Cohen, W. M. "View from the Bench: Patents and Material Transfers." *Science* Vol 309. 23 September 2005.

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[19] Heller, M. A. and Eisenberg, R. S. "Can Patents Deter Innovations? The Anticommons in Biomedical Research." *Science* Vol **280**. 1 May 1998.

Bio
BIOTECHNOLOGY
INDUSTRY ORGANIZATION

Biotechnology Industry Organization
On Research Use Exemptions
July 28, 2005

Overview

In exchange for complete disclosure of an invention, a patent grants the right to exclude others from using the invention for a limited time. This time-tested contract is the cornerstone of technological progress in a free economy, as it provides incentive to research and invent while society gains access to the eventual products and knowledge. Nowhere is this more evident than in the biotechnology industry. Biotechnology offers enormous hope for curing intractable diseases and meeting many of the world's environmental and agricultural challenges, thereby improving the health and well being of people today and for generations to come.

The current intellectual property system in the United States has been instrumental in creating the biotechnology industry and sustaining biotechnology companies. By protecting inventions that are essential to the development of biotechnological products, the patent system's time-limited protection spurs investment into the research and development of technological products, particularly biotechnology products. It is common for a biotechnology company to expend hundreds of millions of dollars and work for more than a decade before it reaps its first dollar of product revenue. The risks are great, and few companies actually succeed in their quest to get products approved by regulatory authorities. Without strong, predictable, comprehensive and enforceable patent protection, it is unlikely that investors would risk their capital or resources to fund biotechnology endeavors. Through patent protection for the molecules that serve as modern biotechnology's foundation (proteins and nucleic acids) the biotech community can invest in the R&D needed to bring these important and innovative healthcare products to market.

BIO members are dedicated to translating cutting-edge technologies into products for use in healthcare, agriculture and the environment to benefit humanity. BIO recognizes the importance of the tools heing used in modern biotechnological research, including those used in the private and public sector to decipher the human genome and other genomes. BIO supports the ability of developers of innovative research tools to obtain patents on their discoveries. BIO also supports the rights of developers to use intellectual property rights to succeed commercially so that investment in needed innovation will continue and society will reap the benefits.

Through their close relationship with the research and academic communities, both public and private, BIO members are dedicated to promoting the larger objectives of scientific progress against disease and famine.

Research Use Exemptions

Exemptions from patent enforcement are rare in U.S. patent law. However, there are two types of existing exemptions that are of importance to BIO members.

One exemption is the judicially created research-use exemption. This narrow exemption permits making and using a patented invention to better understand **that** invention. It provides that it is not an act of infringement to make and use a patented invention if the use is limited to research or experimentation and the user does not obtain any commercial advantage or benefit.

The courts have interpreted this exemption narrowly. In *Madey v. Duke*[1], the Court of Appeals for the Federal Circuit held that activities that could be construed to have a business-related objective (e.g., publishable research to further a university's prestige, image, & ability to bring in grant money) are considered to be outside the scope of a research use exemption. Thus, academic researchers may be outside the scope of exemption if their activities further the interests of their institutions, such as attracting researchers or securing research grants. As a practical matter however, a patent owner will generally not enforce his patent against a researcher if the research activities in question do not damage the patent owner's commercial interests.

A second type of research exemption is included in the Hatch-Waxman Act of 1984[2]. This exemption allows making and using a patented pharmaceutical compound or device to collect data for submission to a U.S. Government regulatory agency (typically for a generic drug manufacturer to submit to the FDA). This "safe harbor" is intended for individuals or entities making and using patented materials for uses "reasonably related" to the development and submission of information to the government. In *Merck v. Integra*[3], the Supreme Court held that a certain amount of experimentation using a patented invention falls within the "safe harbor" provision of the Hatch-Waxman Act as long as the experimentation is reasonably related to the development and submission of data for the government regulatory agency. At the same time the Court held that not all experimentation falls within the safe harbor.

BIO believes that taken together, existing practice[4] and law[5] [6]pertaining to research use of patented inventions is appropriate and provides the appropriate balance between product development and research.

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[1] John M.J. Madey, Plaintiff-Appellant, v. Duke University, Defendant-Appellee., 307 F.3d 1351; 2002 U.S. App. LEXIS 20823; 64 U.S.P.Q.2D (BNA) 1737

[2] PL 98-417

[3] Integra Lifesciences I, Ltd. and The Burnham Institute, Plaintiffs-Cross Appellants, and Telios Pharmaceuticals, Inc., Plaintiff-Appellee, v. Merck KGaA, Defendant-Appellant, and The Scripps Research Institute and Dr. David A. Cheresh, Defendants. 331 F.3d 860; 2003 U.S. App. LEXIS 11335; 66 U.S.P.Q.2D (BNA) 1865

[4] Existing material transfer and licensing practices.

[5] *Merck v. Integra*

[6] *Madey v. Duke*

Gene Patenting FAQ'S

What is a patent?

A patent is an agreement between the government and an inventor whereby, in exchange for the inventor's complete disclosure of the invention, the government gives the inventor the right to exclude others from using the invention in certain ways. The property right granted is quite different from what we typically think of when we own land or other real property. A patent does not provide the right to make, use, offer for sale, sell or import, but the right to stop others from making, using, offering for sale, selling or importing the invention.

Can living things be patented?

Some, but not all, living things. The United States Patent and Trademark Office, PTO (the agency charged with granting patents) enforces strict standards, set by Congress, on what can be patented. Like any invention or discovery, a living thing must be "new", non-obvious, and useful in order to be patented. More importantly, living organisms under consideration for patenting cannot be those that occur or exist in nature "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 USC 101. One cannot obtain a patent on just any living creature, such as a mouse, because mice have been around for a long time. If, through manipulation of genes, someone makes a kind of mouse that never existed before, however, then that kind of mouse might be patentable.

For example:

- **Microbes**

  As long ago as 1873, Louis Pasteur received a US patent for yeast "free from organic germs or disease." With the growth of genetic engineering in the late 1970's, the patentability of living organisms was re-examined, and confirmed. A landmark case involved Ananda Chakrabarty's invention of a new bacterium genetically engineered to degrade crude oil. In 1980, the US Supreme Court clearly stated that new microorganisms not found in nature, such as Chakrabarty's bacterium, were patentable. Chakrabarty received a patent in 1981 (US Pat. No. 4,259,444). In its Chakrabarty decision, the US Supreme Court stated that "anything under the sun that is made by the hand of man" is patentable subject matter. Therefore, if a product of nature is new, useful and nonobvious, it can be patented if it has been fashioned by humans.

- **Plants**

In 1930, the US Congress (Congress) passed the Plant Patent Act, which specifically provides patent protection for newly invented plants that are asexually reproduced. In 1970, Congress provided similar protection for newly invented sexually reproduced plants.

- **Animals**

In the 1980s, the question of whether multicellular animals could be patented was examined. The key case involved a new kind of "polyploid" oyster that had an extra set of chromosomes. This new, sterile oyster was edible all year round because it did not devote body weight to reproduction during the breeding season. The PTO found that such organisms were in fact new but this particular type of oyster was determined to be obvious, and thus into patent was allowed. Nonetheless, the polyploid oyster paved the way for the patenting of other nonnaturally occurring animals. In 1988, Philip Leder and Timothy Stewart were granted a patent on transgenic nonhuman mammals (U.S. Pat. No. 4,736,866) that covered the so-called Harvard mouse, which was genetically engineered to be a model for the study of cancer. The PTO does not allow anyone to patent a human being under any circumstances. A 1987 PTO memo issued by Donald J. Quigg, Assistant Secretary of Commerce and Commissioner of Patents and Trademarks, states, "A claim directed to or including within its scope a human being will not be considered to be patentable subject matter." Accordingly, since 1987, the PTO has rejected any application that encompasses a human being.

- **Natural Compounds**

Natural compounds, such as a human protein or the chemical that gives strawberries their distinctive flavor, are not themselves "living," but do occur in nature. Thus, they are new, and can be patented, only if, they are somehow removed from the setting in which they naturally occur (*isolated*). Therefore, a compound that is *purified* away from a strawberry, or a protein that is *purified* away from the human body can be patented *in its purified state* (provided that, the purified, e.g., protein or compound, also meet the other requirements for patentability, as well). Such a patent would not cover the chemical while in the strawberry or the protein while in the person. Such a patent would not cover the strawberry or the person. The USPTO does not allow anyone to patent a human.

What is a gene?

A gene is the fundamental physical and functional unit of heredity. It is made up of tightly coiled threads or polymers of deoxyribonucleic acid (DNA). DNA is an informational molecule and is made up of four distinct nucleotides: deoxyadenosine (A), deoxyguanosine (G), deoxythymidine (T), and deoxycytidine (C). It is the nonrandom order of these individual "bases" that results in DNA being an informational molecule. However, in and of itself, DNA has no functional property. It is a chemical that, when placed in an appropriate environment, will direct the synthesis of particular and specific proteins, which make up the structural components of cells, tissues and enzymes (molecules that are essential for biochemical reactions). Organisms, from single-celled protozoans to far more complex human beings, are made up of cells containing DNA and associated protein molecules. The DNA is organized into structures called chromosomes, which encode all the information necessary for building and maintaining the organism. A DNA molecule may contain one or more genes, each of which is a specific sequence of nucleotide bases. It is the specific sequence of these bases that provides the exact genetic instructions that give an organism its unique traits.

Can genes be patented?

Isolated and *purified* genes are patentable inventions if they meet the patentability requirements of Title 35 (including being novel, nonobvious, adequately described and useful). It is difficult to identify genes and even after we recognize them, it is very difficult to isolate them and put this information to use.

Gene and nucleic acid-based patents have helped attract the biotechnology and pharmaceutical industry's interest in the development of gene-based therapeutics, diagnostics and processes. For example, the isolated and characterized gene associated with a certain type of breast cancer, Her-2, was patented after years and millions of dollars spent in its identification, isolation and characterization. This discovery and the patents protecting its various aspects, enabled companies to develop therapeutics and diagnostics for breast cancer.

Are patents granted on an individual's genes?

No. Patents do not provide any rights to a person or to the genes in his or her body. Instead, patents are granted on *isolated* genes and gene products that have real-world applicability. That is, the patents cover genes and gene products that could be obtained from any person, for example, from a blood sample. Genes are not unique to an individual. Two unrelated people with brown hair may have the same gene that causes their respective locks to be brown. Or two women may have the same mutant gene that makes them susceptible to breast cancer. In that sense, a gene is generic and could be obtained from any number of people who posses that gene. (What makes an individual unique is the collection of genes that make up their DNA). As previously mentioned, patents may also cover genes of microbes as well as genes from animals and plants.

When considering the patentability of nucleic acids, which are the building blocks of genes, one must take into account the nature of the object for which protection is being sought. A nucleic acid, regardless of its source, is chemically indistinguishable from any other nucleic acid. While its sequence of bases may change, there is no *a priori* means of establishing its source. Human DNA is no different, at least chemically, from that of a bacterium.

If one were presented with a nucleic acid, its sequence could be chemically characterized, and any protein that it might encode could be determined. However, it would not be possible to ascertain what species the DNA came from. In fact, DNA as an isolated molecule does not exist within living cells. It is always associated with various other molecules, such as proteins, sugars and fats. It is well established that subject matter that is a product of nature is not eligible for patent protection. However, isolated nucleic acids do not exist in nature.

How will the patents on DNAs, RNAs, and their correlates help society?

Gene and nucleic acid-based patents have helped attract the biotechnology industry's interest (and the pharmaceutical industry's interest) in the development of gene-based therapeutics, diagnostics and processes. Many, if not most, human diseases have their roots in our genes. More than 4,000 diseases are suspected to stem from mutated genes inherited from one or both parents. As of April 2000, 1,792 individual genes had been linked to disease, including common disorders such as heart disease and many cancers. In addition, discovery of new genes holds promise for new treatments, diagnostics, predictive tests, and agricultural and environmental innovations. However, in most cases, these discoveries will not be further developed if they are not patent protected.

Without patents, these discoveries will remain just that, discoveries sitting on laboratory shelves, and society will miss out on the public benefit that could have come from such discoveries. Without the ability to protect core biotech inventions such as DNAs, RNAs (ribose in place of deoxyribose, uracil (U) in place of thymine (T)) and their correlates, the prospect of investing in biotech is so risky that investors will choose other industries and technologies in which to invest. The road to putting a biotech product on the market is long (10 to 14 years) and expensive (hundreds of millions of dollars) and, that, only a small percentage (one out of 1,000) of biotech products ever make it to clinical trials and, of those, an even smaller number (one in five) ever make it to the market. These odds are astronomical, and patents provide the investor with an assurance that if anyone benefits from the research, it will be the party that took the risk to invest in that research. Without patents on biotech inventions, investing in biotech would be akin to a donation rather than an investment and investors will choose other industries and technologies in which to invest. The lack of availability of patents for biotech inventions will be detrimental, not just to the growth of, but also to the survival of, the biotechnology industry.

Mr. BERMAN. Well, thank you all very much.

I will recognize myself for 5 minutes to begin the questioning process.

Dr. Sung, you proposed in your written testimony a very specific legislative proposal that creates a research use exception. One problem I have heard often in designing a research use exception is being able to draw a bright line between commercial use and a research use of an invention. How did your proposal deal with that issue?

Mr. SUNG. Well, Congressman, I should say that the research use proposal that I laid out in my written submission was used as a piece for further discussion points about that very aspect of it. I do not think that it has been traditionally very easy to make that delineation between commercial and noncommercial use. In fact, a focus of the Federal Circuit opinion in *Madey v. Duke* related to that difficulty.

That being said, the proposal, therefore, takes it and makes it a selective opt-in process whereby it is a self-identification issue on the part of entities interested in engaging in that type of "academic" research use, and to the extent they are willing to self-identify, there would need to be some transparency and accountability for what they plan on doing through the submission of a detailed research plan.

This is not meant to put both the academics and the private industry at odds, but, hopefully, to help foster a more open working relationship between the two for that purpose.

Mr. BERMAN. So the researcher opts in and then has some kind of transparent process submitted to, what, the PTO or another authority?

Mr. SUNG. Actually, it could be a notice directly to the patent owner for that purpose and, again, to facilitate the dialogue. Now some may say that it is problematic because oftentimes researchers would not know about a patent in existence, much less the patent owner, and the reason this is drafted as an opt-in procedure is you could certainly rely on status quo and conduct your affairs accordingly.

Mr. BERMAN. Mr. Kushan, you say that any change to the law regarding gene patents would negatively affect expectations by investors in biotechnology companies. You also indicate that the biotechnology industry has had a long tradition of refraining from asserting their patents against universities, and you point to data that supports this.

Since the biotechnology industry does not sue universities that are making research use of their gene patents, would legislating a clear research use exception upset investor expectations? Wouldn't an explicit research use exception for gene patents just codify an already existing practice and, therefore, be of no real importance to investors?

Mr. KUSHAN. Well, as your past 3 years of effort in carefully drafting patent reform has shown, the words you choose to articulate that line will be very difficult to write down and to make sure they do not have an overbroad or underbroad or unintended consequences.

Mr. BERMAN. We will not use a second window. [Laughter.]

Mr. KUSHAN. I think it is fair to say that this has been kind of an academic question that we have seen for the past 15 years, whether it is necessary to create this kind of statutory bright line to shield purely academic research. One of the challenges we see, is that we very infrequently see purely academic research.

I think one concern that can immediately come up is if you have an academic researcher who is sponsored by your biggest competitor running programs intending to make an infringing product, we would not want to see a statutory research exemption somehow shield that person from the commercial liability they are going to create, and I think as you go through some of these types of scenarios——

Mr. BERMAN. Why would it? Take Dr. Sung's formulation. The researcher opts in and then tells the patent holder, even though he is being asked to do this by the potential competitor, exactly what he is doing, and the patent holder is sitting there watching to see the day it goes from research into commercial development and whacks him not only for infringement, but for breach of contract or whatever.

Mr. KUSHAN. Well, I will go back to kind of whether that would ever happen. First, there are two scenarios that are out there on this example.

One is that a researcher who is doing purely academic research is going to be concerned about a patent and liability from that, and I do not think there are many researchers who do purely academic research that believe that they are at risk.

The second scenario is if there is really a commercial motivation driving that researcher, putting yourself squarely in the headlights of a patent owner would not be recommended by most attorneys representing the company that is sponsoring that research because it will create unnecessary risks.

I think as a practical matter, we see very few instances of patent owners going after purely academic research, both because there are very limited damages at the outset. You know, the work that is being done does not reflect the kind of scale——

Mr. BERMAN. Well, my time has expired, but——

Mr. KUSHAN. Yes, I am sorry.

Mr. BERMAN. You say they very rarely go after purely academic research, and then you say but they really do not do purely academic research.

Mr. KUSHAN. Well, that is part of the challenge of drawing that line you are trying to draw. I think if it is truly academic research, there is nothing they should be concerned with. If it is something that is not—if it is a sheep in wolf's clothing or a wolf in sheep's clothing—then you should not really be shielding that activity under a research exemption because it is not appropriate to do that. That is actually commercially competitive types of scenarios.

Mr. BERMAN. Thank you.

Mr. Coble?

Mr. COBLE. Thank you, Mr. Chairman.

Let me direct this question to all the witnesses.

Are most of the complaints about gene patents based on isolated incidents or anecdotal evidence? The appendices of Dr. Grodman's testimony cite some disturbing cases, and I am wondering is there a systematic problem with the exclusive licensing of genetic associations.

Mr. Grodman, why don't I start with you?

Dr. GRODMAN. Thanks.

In the testimony, we both have in there, both peer-reviewed articles. There is one article, that from JAMA, that talks about breast cancer specifically and talked about in those areas where there were two genes that were found out that scientific research said that there were other areas, other insertions, genetic arrangements and mutations that, in fact, that 17 percent of the cases in which it seemed to be negative were, in fact, positive under the light of new studies. But in the cases of the one laboratory doing the test, it was not the same incentive or urge to be able to go up and update the test, as if there was another laboratory that was keeping it up to date.

There also were in there specific cases when results come back in an indeterminate manner, which is something that no degree of regulation could attach, could be able to deal with, that in those cases, it is up to between the referring geneticist and the doctor in the laboratory to come up with a satisfactory result, and in that case, that geneticist who referred the test had nowhere else to go for the test.

So the concern is that exclusive licenses in diagnostic gene testing, we believe, does lead to a situation of where there is no proper competition or urge to produce a better service.

Mr. COBLE. Mr. Kushan, let me ask you service this. What would happen to the biotechnology industry if the Federal Government exercised march-in rights on a regular basis, A, and should the standards of section 203 of the Patent Act be amended to encourage greater use of march-in rights?

Mr. KUSHAN. Those are two difficult questions, and I will do what I can to respond to that.

Mr. COBLE. Well, you are a Carolina man. That is why I put it to you.

Mr. KUSHAN. Thank you. Notice my Carolina blue tie.

I think the first question of the use of the march-in authority would have a fairly significant chilling effect on the biotech industry, in part because the political decisions that might drive use of that authority are very scary to companies that have invested money in developing a product. The idea that you are going to do all this work, spend all this money, finally reach the market, and then at the back end of your business model, an uncertainty that you could not have imagined will pop up and deprive you of the patent exclusivity is going to have an impact on use of those funds.

The second part of this is that we have seen the NIH takes steps in the past decade to use their influence without the march-in authority. To set standards of conduct, for example, they developed guidelines relating to use of materials and sharing of research tools when there had been Federal funding involved in that, and that is kind of a better model, essentially putting on the table that before you take funding, you know that there will be conditions attached to it.

I think when you look at the march-in experience, the fact that they have never been used, and that there is so much reticence about going to that as a mechanism, has created a fairly significant set of expectations in the industry that they will not be used at the back end in the commercial setting.

Mr. COBLE. Thank you.

Before my time expires, let me go to Dr. Sung and-or Dr. Soderstrom.

We have compulsory licenses in the Copyright Act. Why shouldn't we have compulsory licenses for patented pharmaceuticals and biologics, either of you two?

Mr. SODERSTROM. I would simply echo many of the comments that Mr. Kushan just made in that when we are negotiating licenses, particularly to start-up companies or biotech companies, this issue comes up all the time. What are the Government reserved rights? What are march-in rights? How often are they used?

It is something that for investors is of extreme concern because of the reasons he pointed out. If they are going to put a significant amount of money at risk over a long period of time in a fairly high-risk technology development exercise, they need some assurance that that investment, if they are successful, would be protected.

Mr. SUNG. I would have little to add to those particular comments, just to say that I think the standard recourse for purposes of saying compulsory licensing is bad defeats investment-backed expectations at the front end.

Mr. COBLE. Quickly, Dr. Grodman. The red light is about to illuminate.

Dr. GRODMAN. It is already on there.

Mr. COBLE. It has illuminated.

Dr. GRODMAN. One point about it: As you mentioned in your opening comments, the cost of getting a new drug to market may well be a billion dollars. What we are talking about, what I am really addressing are diagnostic genetic tests, the cost of which could take from the association between the clinical rendition of this sequence that is done in the university and then licensed out. To have a laboratory to bring up that test, that might be anywhere from $25,000 to $50,000 to, at most with new technologies, may be a quarter of a million dollars. It is not the same investment that we are talking about with therapeutics. It is very, very different.

Mr. COBLE. I yield back, Mr. Chairman. Thank you.

Mr. BERMAN. Thank you.

We will have a chance to explore that specific subject you are raising later in the third and fifth rounds of questioning.

Mr. Issa?

Mr. ISSA. Thank you.

The fifth round is where I get my really tough questions in.

You know, I looked for something that was akin to this subject. You know, when did we discover something and grant it a patent? And, oddly enough, I found something that was a little bit close, and that was when the product now known as Botox took something that was commonly understood and said, "But you can do it for this. Do what it does, and you can do it for this reason," and it was granted a patent and continues to be an ever more broadly successful product, including for people with migraine headaches now. I think Congress should figure out that Botox is the antidote for what we do.

So, I mean, I see the importance of it, and I guess I will ask two major questions.

Dr. Grodman, this is Coca-Cola. It is a secret. Nobody knows what it is. And I understand that you support the patents, but just because you support it and yet have a problem with the exclusion, if we were to not grant patents in this area, would it be a little bit like this, except we would not see it in the marketplace?

People would discover and then continue to keep it a secret so that they could do the follow-on work. Isn't that a risk we take when we do not patent something which we want discovered, but it could be discovered and kept a secret and, for example, diagnostic centers could preclude you from knowing what you need to know while they know what they need to know and say, "Just send it to us, and we will tell you whether you have this fatal disease."

Dr. GRODMAN. Well, I would probably be scarcely the last one on this panel who would be championing patents. I think that in the medical arena, we do know what the formula, if you will, of Coca-Cola is. It has been well researched and referenced in medical journals. The question is whether or not we are able to go in and have access to that different information.

So I am by no means, for my purpose today, supporting or not supporting patents. What I am supporting is the fact that there needs to be competition that when we have certain information about diagnostics that people can compete over producing a better test.

My own preference is that the information is open and that people do benefit. In a system of what I am addressing, that license for Coke is the best one there is and everyone knows what it is, I am saying, fine, but pay them a license if you want to be able to do it, but be able to allow everyone to be able to enjoy Coke no matter what the outside——

Mr. ISSA. So, essentially, you have to make the argument for a patent. Otherwise, there would be nothing to license. It would just be a secret.

Dr. GRODMAN. I am not making the case for or against patents. My concern is the ultimate amount of patient care and creating the competition for the exclusionary idea that people cannot perform a test.

Mr. ISSA. Mr. Sung, I guess I will switch to you just to see if I can get a dissenting opinion.

If we, in fact, deny patents in this field, don't we induce universities, perhaps the private sector because universities might choose to publish regardless, don't we induce people to cloak discoveries in a way that allow them to further their business practices without ever releasing them? Couldn't you end up with five or ten or 20 different research facilities discovering the same thing, but keeping it to themselves because if they cannot enjoy a period of patent protection, they might as well enjoy a period of exclusivity through nondisclosure?

Mr. SUNG. No, I agree with those comments. I think that what you are risking if you were to deny patent exclusivity in a particular area is to risk that, without that encouragement for disclosure, that there may be, I guess, more of a motivation, if you will, toward keeping something secret for a business purpose, but that would depend in a particular industry on the various market and business approaches. But I do agree that you would be removing the encouragement for disclosure that the patent system was designed to protect.

Mr. ISSA. And, Dr. Grodman, I will go back to you. I will get off Coca-Cola for a moment.

I was an electronics manufacturer with now hundreds, but in those days 37 of my own patents, and I made it a practice not to license anybody. I made it a practice to produce my own products and to provide a superior product based on my patent.

Why is it, you think, that a medical diagnostic company, whether or not they invented it or they licensed it, should not have that same ability to do it, and why do you think that it, per se, causes them not to want innovation? Isn't their clock ticking, and that if there is not an encouragement by the licensee to get the inventor to invent more and to continue, if that encouragement is not there by the large dollars and the ticking clock on the patent, why wouldn't that, in fact, induce good development and good products?

Dr. GRODMAN. I would argue that that is not necessarily the case when it comes to medical diagnostic and genetic diagnostics, that when you go in and have an area which has a clinical association, what you are really doing is not having a product or something that you are going to sell. You are patenting an association, whether it be for a type of arrhythmia in three or four different genes, and if you go in and you will do that test, if you do it without competition, you will perform that test, and if people have that, they will have nowhere else to go for that answer.

Let us say someone else goes in and says, "You know what? There are three or four other genes that we can discover that will make the answer clearer, better for those who are at risk, maybe with medicines they need to be on or not. There is no possible way that a test could be done on those without getting the permission or a license on the original genes. As a result, innovation in that case, gets to be stifled and patient care is affected.

If the second group of people had a license to perform those tests, they can go in and make the ultimate test better. That would be lost if only one person had the innovation.

The example in the testimony that we gave about where there were certain genes about breast cancer that were done, it took 10 years of time for the one company that had the exclusive license to include those other genes to help make the test clearer for risk of breast disease. In a competitive framework, that would not be the case.

I would argue that the genes on products or patents on products or drugs is different than in this case of the diagnostic association between a clinical condition and a sequence. There are fundamental differences which makes it important for multiple people to do the test.

Mr. ISSA. Thank you. I yield back.

Mr. BERMAN. I think we will do a second round.

I have a couple of questions, but let me just make sure I understand. You are not arguing to nullify gene patents? Is there something different between a patent on a gene segment and a patent on a genetic diagnostic test? Are those two different?

Dr. Soderstrom?

Mr. SODERSTROM. No, sir. They are essentially the same. In fact, were we as universities to have that competition on the front end where there are multiple companies that are interested in commercializing these products, that would be a great thing. That is not often the case. In fact, it is seldom the case with universities, and this is another misconception.

We often think of it as there is a patent, and there is a product, and, as you know from your experience, those two things are not necessarily equal and, in fact, oftentimes, we are in the business of aggregating technology so that we can create the product, and that is one of the misconceptions.

So, while I admit that there have been some examples where we probably as universities could have done licenses differently in hindsight, oftentimes we are not in that admirable position. We are looking toward trying to induce somebody to invest in the technology and trying to bring it into a product form as quickly as possible.

So we do take a nuanced view. We do not necessarily always grant across-the-board licenses. We divide it up into fields of use, for example.

Mr. BERMAN. For me, I want to really get it down to something so simple that I can pretend to understand it. I think of a medicine, and biotechnology produces medicines, and then I think of tests, which determine whether or not you have something, or you have a predisposition to something or a genetic makeup that might mean a higher likelihood of getting something. Should I be thinking about patents in the context of these different things, or does it all blur into one?

Mr. SODERSTROM. Ultimately, they are the same. They are products that embody claims to a patented invention, and to the extent that you deliver that in a pill bottle or to the extent that you deliver that in a set of reagents that are going to be mixed with a patient's blood and then spotted on a slide, they are no different.

Mr. BERMAN. In other words, they may have different goals, treating versus diagnosing, but——

Mr. SODERSTROM. When we are presented with a discovery of a new gene that affects a disease category, there are usually four different sets of claims that you write for it. One is the use of the protein that is expressed as a therapeutic, the gene itself as a potential diagnostic, the gene potentially as an antigen that would be used in a vaccine or other prophylactic, and then the third is as a research reagent for the discovery of other things. Those are the four major claims that are on all DNA-based sequences that we typically use. How they——

Mr. BERMAN. You mean it is sort of boilerplate?

Mr. SODERSTROM. It is pretty close nowadays, yes. It is fairly routine. It is still expensive, but it has become much more routine.

Mr. BERMAN. All right. Then I will ask at least one other question that I wanted to ask before I went down this road.

Mr. Kushan, why wouldn't BIO support the use of march-in rights in the kind of case that Dr. Grodman is talking about, where the need to have others provide genetic tests is great? Again, I guess some of that depends on how I understand the questions I was asking you.

Can you have march-in rights for this? I guess march-in rights exist. They are just never utilized. But can we encourage the use of march-in rights in this sort of subset of an area where the investment is not billions, it is thousands, tens of thousands, hundreds of thousands to achieve the kinds of purposes that Dr. Grodman was talking about?

Mr. KUSHAN. Well, I think your earlier question is getting to the challenge that is at the root of this problem. The patents that issue are going to have claims on nucleic acids corresponding to a gene that, you know, you discovered. That single patent is going to protect many different potential applications.

One might be development of a method of making the protein which then becomes a drug. Another might be using this clinical diagnostic setting where you are going to be screening and trying to determine if that gene is present in a sample. I do not know what another application might be, but for the purposes of this process, you are talking about the single patent.

Putting a condition through march-in rights on limiting the use of that patent right is the thing that cause concern within the biotech sector. The idea that at the back end of the process, once you have reached the market, there is going to be a Government-mediated decision to limit those patent rights, that is, I think, the chilling effect that I was trying to describe before.

Mr. BERMAN. My——

Mr. KUSHAN. I think——

Mr. BERMAN. I am sorry.

Mr. KUSHAN. No, I think one of the other questions that I wanted to address is just can you address the concerns that have been raised in these settings of clinical diagnostic use versus patent rights and product development. I do not think you can do that cleanly through the patent system or by limiting patent rights.

One of the things we always like to point out is that the patent rights are rights over the invention, and if there is conduct or other types of conditions that are seen in the market regarding the behavior of these companies, there are other ways of addressing that, other than through the patent system, and I guess that is one question to tackle, is whether that is something that is worth looking into.

Mr. BERMAN. Mr. Coble?

Mr. COBLE. Thank you, Mr. Chairman.

Because this issue is firing away, I will come back at you with a two-part question. What is your opinion of the biotech examiners at PTO, A, and, B, are they approving overly broad biotech patents similar to what occurred with business method patents in the late 1990's?

Mr. KUSHAN. Well, I was at one point in my life a biotech examiner, and I think for that sector of the Patent Office, I feel like those patent examiners probably are on the higher end of the scale of experience and training of most patent examiners. Many of them have Ph.D.s. They are probably the best of the group over at the Patent Office based on their training, experience, et cetera.

I think the Patent Office is doing the best job I have seen of really tying down our patent claims. I think anybody that works in the area of getting patents out of that group can share my pain of saying that the claims that you emerge with are often viewed to be exceedingly narrow, driven by both the strictness of the examiner's perspective and how the Patent Office uses these significant cases that have come down.

That goes to one of my comments in my testimony. This is one area where you are not talking about a patent that should not have issued. These are patents that are meritorious. They are narrow. They match the contribution in the patent application, and so that is why we are looking at these rights with great interest. They are very strong patent rights that should be respected.

Mr. COBLE. Thank you, sir.

To either of the other three witnesses, gentleman, to what extent are patent pools used today and should the Congress do anything to encourage their use?

Mr. SODERSTROM. Congressman, the use of pooling of patents has become much more routine on universities' parts, but probably the most impressive one is the pharmaceutical industry's patent pooling on snips, the small repeated segments, unique segments in genes that we find.

It has become a reality for most of us in licensing technologies that we only own a small part, in part because of what Mr. Kushan just said, which is our claims have become significantly narrowed, and that is a significant reality in the last 6 or 7 years, that it has become much more difficult to get broad claims in the Patent Office.

In my case at my university, it is very frequent, probably 10 to 20 percent of the time, we are putting together intellectual property, not just from Yale, but from other university colleagues to try to put together a package which then could be licensed.

It is not difficult to do. It has become relatively routine, and I do not see it as being a significant barrier to entry for a product.

Mr. COBLE. Yes, sir?

Dr. GRODMAN. I cannot comment on what it is like in the academic environment. In the commercial environment, you know, it is a noble attempt to be able to overcome a problem, but it is something which has not taken hold. I mean, there are many cases in which we can talk about where some genes will diagnose a condition and three other genes may diagnose it better or differently, and in those cases, there is very little camaraderie or ability to be able to share information, often, when that happens, causing conflict. It is a noble attempt, but it has not helped the diagnostic arena in a commercial environment.

Mr. COBLE. Dr. Sung, do you want to weigh in before my time expires?

Mr. SUNG. Only to say that what we have here as a result for looking at patent pools is that DNA is a de facto industry standard for biological sciences. You cannot wake up tomorrow and say, "I will not use DNA for these purposes," and so for that reason, the ability to design around in this field is very different than you might see in other mechanic or electrical technologies where patent pools first grew up. So I think there is a need for this in many instances that are more heavily——

Mr. COBLE. Thank you.

Thank you, gentlemen.

I yield back, Mr. Chairman.

Mr. BERMAN. Mr. Issa, here is my problem.

Mr. ISSA. Yes, sir.

Mr. BERMAN. I have to go to the DOD Authorization Conference Committee to push language that the Foreign Affairs and Judiciary Committees are both recommending on the issue of Iraqi refugees. They want me there now for this Conference Committee. My inclination would be to give either of you the gavel to let you keep going, but I am told I am not allowed to do that.

Mr. ISSA. Yes, the Senate has gotten in trouble for doing that, too.

Mr. BERMAN. To give it to a Republican?

Mr. ISSA. Giving it to me. [Laughter.]

Mr. ISSA. And I did not even abuse it. Okay. You want me to wrap up?

Mr. BERMAN. So, I mean, the fact is I have five or eight more questions I want to ask all of you, but I am not going to be able to do it during this process. I would hope you would allow us to be in touch with you to pursue some of these things because we have in some cases just touched the surface, and we intend no commercial use of our research. [Laughter.]

Mr. ISSA. Thank you, Mr. Chairman. I will be quick.

Dr. Soderstrom, there was an earlier statement that somehow patents were barring people from doing follow-on research to discover new genes. In your experience, is that incorrect?

Mr. SODERSTROM. That is incorrect.

Mr. ISSA. Okay. So Yale University does not feel that even if somebody over here has an exclusive license, that you read the patent, that it allows you to take what they have done and look at it for your follow-on work. You just cannot incorporate it in your later release. Would that be fair?

Mr. SODERSTROM. Two points: One, is there is no tendency to look at patents prior to conducting research. At Yale, university faculty members are free to pick any area of inquiry. Second, in terms of the discovery that they ultimately make, we do do novelty searches to see if there is other intellectual property——

Mr. ISSA. Sure.

Mr. SODERSTROM [continuing]. And in those cases, we may choose not to patent simply because we do not see the point, and we would just encourage publication as soon as possible. If we do think that it would be a significant improvement, we usually would approach whoever has the exclusive rights.

Mr. ISSA. Okay. Now this is an academic question, but, for me, it was not academic. My experience has been that exclusivity, being excluded from somebody's invention, caused me to, in fact, figure out a way to skin the cat differently.

I am not in your industry. I am not in your academic endeavors, but isn't it somewhat true in all areas of endeavor that what you do not have access to—and, Dr. Sung, Larry, I saw you perk up on this, so you get first thing—isn't it true that in a sense there is a benefit to exclusivity which is it causes people to go elsewhere and discover other things or around it? Isn't that an experience that even in medicine goes on?

Mr. SUNG. Well, I do think as a generality the patent system is designed to encourage design-around efforts and forward progress as a result of those efforts. I do think that in certain instances, again, because we are talking about genomic information here, the ability to do so may be somewhat stricter and harder to do. So I think there are instances where there may be blocking patents that might issue to this that are impossible as a technological matter to design around.

Mr. ISSA. Okay.

Mr. SUNG. But I think your general proposition is correct.

Mr. ISSA. And isn't the pooling that has gone on, to a certain extent, the result of those blocks causing people to go to other areas, create, if you will, block backs that then lead to the pooling being a necessity so that you have an ability to invent in an area in which very little is known?

Doctor?

Mr. SODERSTROM. That has certainly been our experience. That is what we have recognized, because people see it as a utility, as an opportunity to get around some of the things that are blocking them.

Mr. ISSA. Same? Same?

Dr. GRODMAN. No, I would disagree with that.

Mr. ISSA. So we only have three out of four. Okay. Well, you know that we can get a suspension pass with that here. Time is limited for the Chairman, too, so I appreciate that we sort of have a disagreement, but at least we got that out, as to what the value of exclusivity is potentially.

Thank you, Mr. Chairman.

Mr. BERMAN. All right.

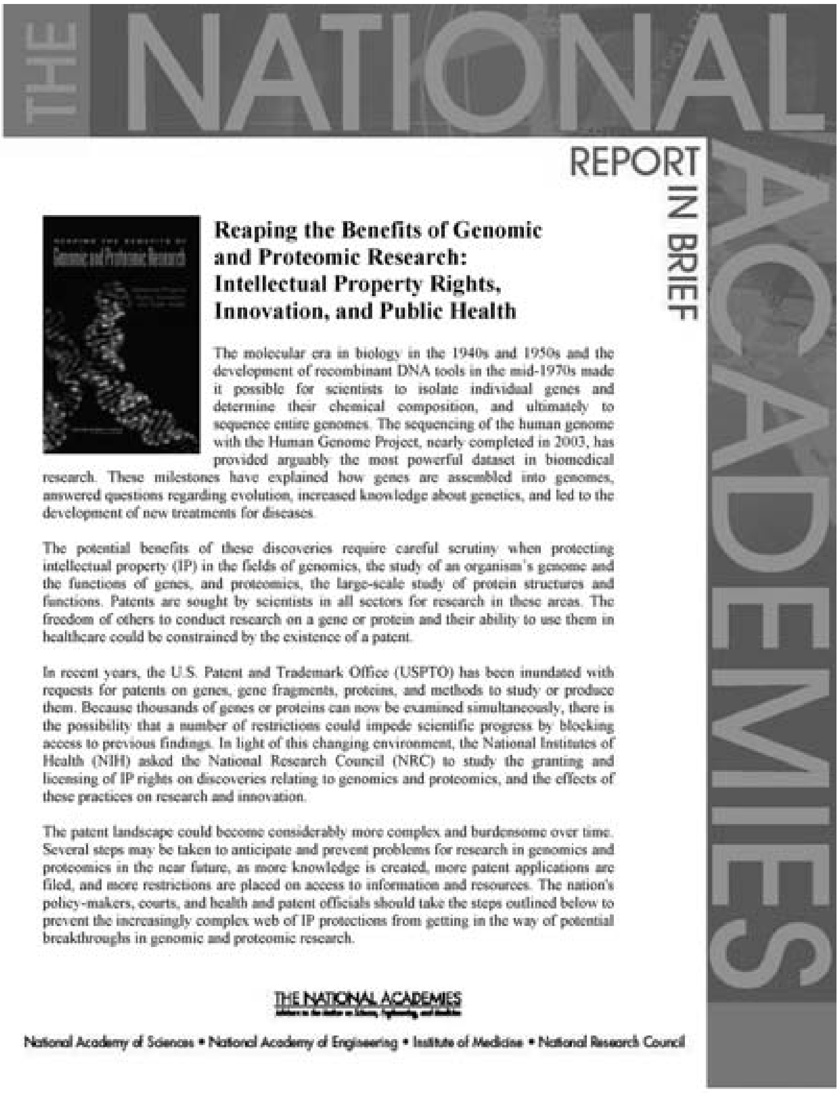
With great regret, I have to adjourn because of the way this place works, but I do appreciate you coming, all your efforts, particularly the effort some of you made coming a ways to testify, and we will be following up individually and perhaps with questions.

Thank you very much.

[Whereupon, at 3:28 p.m., the Subcommittee was adjourned.]

APPENDIX

MATERIAL SUBMITTED FOR THE PRINTED HEARING RECORD



THE NATIONAL ACADEMIES

REPORT IN BRIEF

Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health

The molecular era in biology in the 1940s and 1950s and the development of recombinant DNA tools in the mid-1970s made it possible for scientists to isolate individual genes and determine their chemical composition, and ultimately to sequence entire genomes. The sequencing of the human genome with the Human Genome Project, nearly completed in 2003, has provided arguably the most powerful dataset in biomedical research. These milestones have explained how genes are assembled into genomes, answered questions regarding evolution, increased knowledge about genetics, and led to the development of new treatments for diseases.

The potential benefits of these discoveries require careful scrutiny when protecting intellectual property (IP) in the fields of genomics, the study of an organism's genome and the functions of genes, and proteomics, the large-scale study of protein structures and functions. Patents are sought by scientists in all sectors for research in these areas. The freedom of others to conduct research on a gene or protein and their ability to use them in healthcare could be constrained by the existence of a patent.

In recent years, the U.S. Patent and Trademark Office (USPTO) has been inundated with requests for patents on genes, gene fragments, proteins, and methods to study or produce them. Because thousands of genes or proteins can now be examined simultaneously, there is the possibility that a number of restrictions could impede scientific progress by blocking access to previous findings. In light of this changing environment, the National Institutes of Health (NIH) asked the National Research Council (NRC) to study the granting and licensing of IP rights on discoveries relating to genomics and proteomics, and the effects of these practices on research and innovation.

The patent landscape could become considerably more complex and burdensome over time. Several steps may be taken to anticipate and prevent problems for research in genomics and proteomics in the near future, as more knowledge is created, more patent applications are filed, and more restrictions are placed on access to information and resources. The nation's policy-makers, courts, and health and patent officials should take the steps outlined below to prevent the increasingly complex web of IP protections from getting in the way of potential breakthroughs in genomic and proteomic research.

THE NATIONAL ACADEMIES

National Academy of Sciences • National Academy of Engineering • Institute of Medicine • National Research Council

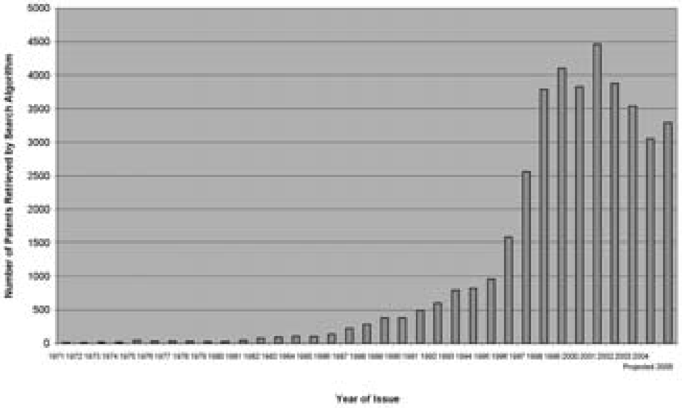


Figure 4-1 Number of DNA-based U.S. Patents (as of June 30, 2005) 2005 Projection is based on mid-year total.
Source: Georgetown University Database

BEST PRACTICES

Many of the potential problems for genomics, proteomics, and IP can be avoided if scientists and institutions follow the best practices already outlined by NIH, NRC, and others to facilitate the free exchange of materials and data.

Foster Free Exchange of Data, Information, and Materials

NIH should continue to encourage the free exchange of material and data among its grantees and contractors. Additionally, NIH should require these individuals to comply with the agency's guidelines for obtaining and disseminating biomedical research resources and for licensing genomic inventions. Industries and nonprofit institutions should standardize and streamline their processes for exchanging biological material or data.

NIH also should adapt and extend the "Bermuda Rules," which were created in 1996 by scientists involved in the publicly funded Human Genome Project. The rules instruct genomics researchers to share their data in a free public database called GenBank. They should be extended to include protein-structure data that NIH-funded centers generate for large projects in genomics. Researchers in both the public and private sectors should make this information freely available in the Worldwide Protein Data Bank, a project overseen by a consortium of international research groups.

Foster Responsible Patenting and Licensing Strategies

NIH has issued two publications, *Principles and Guidelines for Recipients of NIH ResearchGrants and Contracts on Obtaining and Disseminating Biomedical Research Resources* and *Best Practices for the Licensing of Genomic Inventions* that provide guidance to NIH-funded institutions on balancing the need to protect IP rights with the need to broadly disseminate new discoveries and to maximize the public benefit whenever technologies owned or funded by the Public Heath Service are transferred to the commercial sector. NIH should require recipients of all research grants and awards, cooperative agreements, contracts, and intramural research studies to follow these guidance documents. Other funding organizations (such as other federal agencies, nonprofit and for-profit sponsors) should adopt similar guidelines.

In addition, patent recipients should analyze whether further research, development, and private investment are needed to realize the usefulness of their research results and that proprietary or exclusive means of dissemination should only be pursued when there is a compelling need. Also, whenever possible, licenses should be limited to relatively narrow and specific commercial application rather than as blanket exclusive licenses for uses that cannot be anticipated at the moment.

ADAPTING THE PATENT SYSTEM TO GENOMICS AND PROTEOMICS

Some of this research has the potential to blur the boundaries between abstract ideas and applications. USPTO should create a formal mechanism, such as an advisory board of leading scholars in these fields, to inform examiners of new developments and research directions and to improve the understanding of complex and rapidly evolving technologies.

Nonobviousness

To qualify for a patent, an invention must be useful and represent a creative leap; it cannot be obvious to a person of ordinary skill in a given area. When applying the "nonobviousness" standard to genomic and proteomic inventions, USPTO and the courts should consider whether a scientist of ordinary skill would have been able to create a given invention with reasonable expectations of success at the time the invention was made.

Utility Standard

The Supreme Court established a standard in its 1966 decision in *Brenner v. Manson* requiring that a patent applicant show that an invention has "specific benefit in its current form." However, this standard has not been applied in a consistent manner. Investigators and their institutions should avoid seeking patents for genes or proteins whose functions are unknown. These include proteins that are useful for research but do not have therapeutic or diagnostic functions.

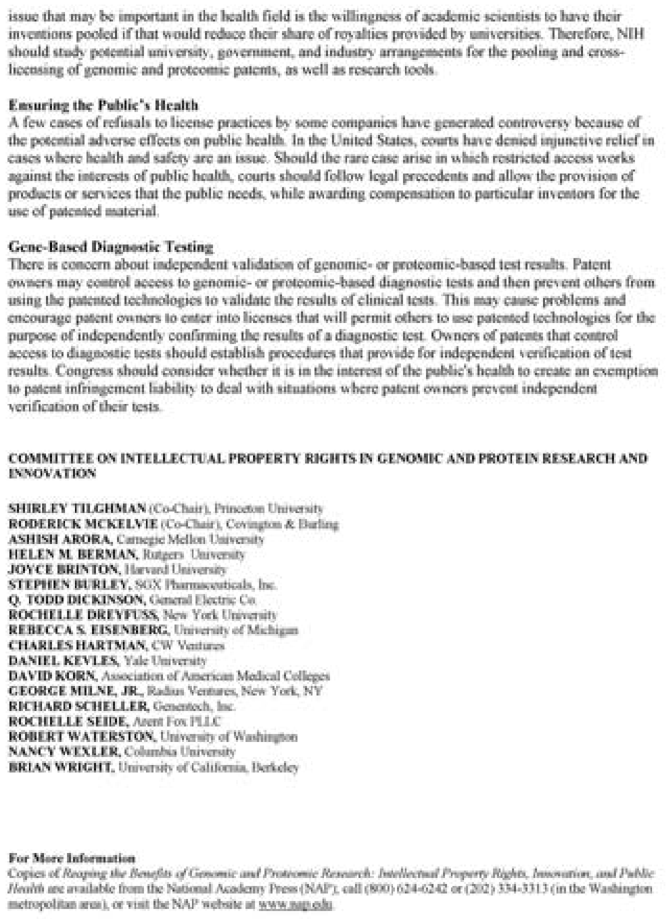
FACILITATE RESEARCH ACCESS THROUGH LICENSING AND SHIELDING FROM LIABILITY FOR INFRINGEMENT

Experimental Use Exemption

A federal appellate court recently rejected the claim that the so-called "experimental use" legal defense shields academic research from patent infringement liability. In the future, academic and other nonprofit research institutions may feel compelled to protect themselves from liability by trying to regulate investigators' behavior. This may hinder research and fail to prevent legal problems because researchers are often unable to determine how existing patents apply to their work. It is also possible that patent holders, knowing that universities do not currently have legal protection from such liability, could increase demands for patent-licensing fees or dictate other terms that would burden the research enterprise. The situation could worsen over time as licensing restrictions imposed by patent holders increase. Congress should consider legislation that would allow scientists to conduct research on patented inventions in order to discover novel uses or improvements without fear of liability for patent infringement.

Patent Pooling

A patent pool is an agreement between two or more patent owners to license one or more of their patents to one another or third parties. Patent pooling is an approach that might address some issues of access to patented upstream technology and its possible applications to biomedical research and development. One



issue that may be important in the health field is the willingness of academic scientists to have their inventions pooled if that would reduce their share of royalties provided by universities. Therefore, NIH should study potential university, government, and industry arrangements for the pooling and cross-licensing of genomic and proteomic patents, as well as research tools.

Ensuring the Public's Health

A few cases of refusals to license practices by some companies have generated controversy because of the potential adverse effects on public health. In the United States, courts have denied injunctive relief in cases where health and safety are an issue. Should the rare case arise in which restricted access works against the interests of public health, courts should follow legal precedents and allow the provision of products or services that the public needs, while awarding compensation to particular inventors for the use of patented material.

Gene-Based Diagnostic Testing

There is concern about independent validation of genomic- or proteomic-based test results. Patent owners may control access to genomic- or proteomic-based diagnostic tests and then prevent others from using the patented technologies to validate the results of clinical tests. This may cause problems and encourage patent owners to enter into licenses that will permit others to use patented technologies for the purpose of independently confirming the results of a diagnostic test. Owners of patents that control access to diagnostic tests should establish procedures that provide for independent verification of test results. Congress should consider whether it is in the interest of the public's health to create an exemption to patent infringement liability to deal with situations where patent owners prevent independent verification of their tests.

COMMITTEE ON INTELLECTUAL PROPERTY RIGHTS IN GENOMIC AND PROTEIN RESEARCH AND INNOVATION

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For More Information

Copies of *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health* are available from the National Academy Press (NAP), call (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area), or visit the NAP website at www.nap.edu.

Advancing Excellence

College of American Pathologists

Statement to the
U.S. House of Representatives Subcommittee on Courts, the Internet and Intellectual Property

Hearing on "Stifling or Stimulating—The Role of Gene Patents In Research and Genetic Testing"

October 30, 2007

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THE COLLEGE OF AMERICAN PATHOLOGISTS

The College of American Pathologists, representing more than 16,000 physicians who practice clinical and/or anatomic pathology appreciates the opportunity to submit comments to the House Judiciary Subcommittee on Courts, the Internet, and Intellectual Property regarding an issue of critical importance to pathologists and the patients they serve—access to genetic testing.

Our member pathologists practice in community hospitals, independent clinical laboratories, academic medical centers and federal and state health facilities.

Pathologists play an integral role in health care as physicians who obtain and interpret data as the result of examination of tissues, blood, and other body fluids for diagnosis and patient care. The mission of the College is to represent the interests of patients, the public, and pathologists by fostering excellence in the practice of pathology and laboratory medicine worldwide.

IMPACT OF GENE PATENTS ON MEDICINE AND HEALTH CARE

The current scientific revolution in genetics promises extraordinary advances in clinical medicine. As the medical specialists in the diagnosis of disease, pathologists recognize that genetic testing is an area of growth and change for pathology and medical practice now and in the decades to come. The research, development, and practice of genetic testing in academic and other medical centers is essential to medical progress, the training of physicians, researchers and health-care professionals, and the continued improvement of the quality of medical care. Most discoveries of human or pathogen genes can be effectively translated into gene-based diagnostic test services without the incentives provided by patents or exclusive license agreements. Pathologists therefore have a keen interest in ensuring that gene patents do not restrict the ability of physicians to provide quality diagnostic services to the patients they serve.

Gene patents pose a serious threat to medical advancement, medical education, and patient care. When patents are granted, subsequent exclusive license agreements, excessive licensing fees, and other restrictive licensing conditions prevent physicians and laboratories from providing genetic-based clinical testing services. As a consequence, patient access to care is limited, quality of patient care is jeopardized, clinical observations as the basis for new discoveries are compromised, and training of health care providers is restricted.

Throughout history, medical discoveries have progressed from the discovery of basic anatomy to histology and cytology—none of which are patented—to the more recent discovery of genes. The trend of using patents to monopolize gene-based testing services is a radical departure from historical precedent in clinical laboratories, and it works against the goal of making these procedures widely accessible and affordable for the public. Especially troubling is the fact that under patent protection, the increasing understanding of the utility of the test, as well as the underlying disease processes, also becomes proprietary, thereby imposing a profound change in how the profession and the public acquire knowledge about these rapidly evolving tests, the diseases diagnosed by the tests and their clinical utility.

The patent system in the United States generally encourages entrepreneurs to make new discoveries and to benefit directly from making their efforts broadly accessible. Limitations in how this patent system is applied to patents of genes compromises medical progress and access to new gene-based tests. The patent system should be reexamined to ensure the public interest in improving healthcare decisions based on gene-based tests and access to those tests.

Physicians and scientists can easily and rapidly translate the fundamental genetic information derived from sequencing the human genome into diagnostic genetic tests and use these tests for patient care. Because information about gene sequences is so fundamental to understanding specific diseases, patent holders can essentially gain ownership of diseases through patents. Exclusive or restrictive license agreements on gene-based tests have been used to prevent physicians and clinical laboratories from performing genetic tests as diagnostic medical procedures. Patients suffer because diagnostic test services are less readily and affordably accessible.

Medical education and research related to laboratory testing also are threatened. The National Academy of Sciences Committee on Intellectual Property Rights in Genomic and Protein Research and Innovation last year recommended in a report that policy-makers take appropriate steps to prevent the increasingly complex web of intellectual property protections from impeding potential breakthroughs in genomic and proteomic research. The report suggests several approaches to improving public access to patented inventions. Specifically, it recommends that Congress consider legislation to exempt research on certain aspects of patented technologies or inventions from patent-infringement liability, with the goal of promoting scientific discovery. The report also recommends that owners of the patented technology behind certain gene-based diagnostic tests should establish procedures that allow other clinicians to validate test results. If these patent holders do not take this step voluntarily, the report suggests that Congress consider, in the interest of public health, whether work to validate such results should be shielded from liability. This sole clinically-focused recommendation falls short, however, in recommending specific protections for physicians and other providers of clinical laboratory services against gene patent infringement enforcement. The College has supported policy recommendations and advocated for legislation in Congress that would extend certain protections to laboratory physicians.

In 1996, Congress recognized that medical procedure patents might impede the advancement of medicine, curtail academic access, place unreasonable limits on the research community, and interfere with medical education and the quality of care provided to the patient. As a result, in October 1996, legislation was signed into law (Frist-Ganske Amendment, 35 USC Sec. 287) that permanently precludes the filing of infringement suits against physicians and other medical practitioners for the performance of "medical activities" that would otherwise violate patents on medical or surgical procedures. A "medical activity" is broadly defined to include the performance of a medical or surgical procedure on a human body, organ or cadaver or on an animal used in medical research. However, the Act does not explicitly affect enforcement of biotechnology patents or extend to clinical laboratory services. With the advent of new and innovative approaches to gene based diagnostic testing, and the promise of enhanced and expanded diagnostic testing, laboratory services and clinicians should have the same protection from patent infringement as other medical providers and procedures.

Because of this oversight, medical practitioners who perform tests to diagnose genetic disease have received “cease and desist” notification letters from gene patent holder’s indicating that continued patient testing would be a patent infringement. Examples of diseases where testing has been halted due to patent enforcement include breast cancer, Alzheimer disease, Canavan disease, and Charcot-Marie-Tooth disease. To address this issue, the Frist-Ganske law should be amended to protect clinical laboratory medical practitioners from patent infringement - just as other medical providers are protected. This would ensure that gene based diagnostic test services, which are part of medical practice and increasingly important, can be performed without fear of reprisal for the benefit of patient care, medical training, and medical research. Additionally, the College supports H.R. 977, the *Genomic Research and Accessibility Act,* introduced by Congressman Xavier Becerra (D-CA) and Congressman Dave Weldon (R-FL) that would prohibit patents from being obtained for a nucleotide sequence, or its functions or correlations, or the naturally occurring products it specifies.

In summary, we are facing the unprecedented situation in which a single patent owner can prevent physicians throughout the country from performing diagnostic procedures that use certain gene-based tests. This sets an extraordinary and dangerous precedent for patients and all of medicine, and strays from the constitutional and social purpose of the patent system to promote progress. Therefore, the College believes that current practices in the patenting and licensing of genetic sequences must be reexamined to ensure that gene based diagnostic tests are widely available and affordable for the greatest public benefit.

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